

The Forgotten Past Inspiring the Future: Revisiting the Potential of Psilocybin Therapy

by

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Abstract

In this paper, I explore the use of psilocybin-assisted therapy while working with cancer patients and individuals struggling with treatment-resistant anxiety, depression, and substance use.

Current methods of treatment for these populations have had limited success and new research in this area is limited. Psilocybin-assisted therapy is a novel and unique form of treatment that approaches these issues from a new perspective with research-supported efficacy. Individuals who have experienced psilocybin-focused treatment report experiences that are life-changing and persist over long-term follow-ups in the research. Experiences that are reported as mystical-like or spiritual in nature are correlated with more significant improvement in the studies. Psilocybin can act as a brain 'reset' for individuals with rigid thinking, rumination, and those who feel pessimistic that positive change is possible.

Psilocybin-assisted therapy could also be used as an alternative to pharmacological treatments based on the evidence of minimal side effects and continued impact months after a single high dose therapeutic session. There is also a movement towards the use of psilocybin in a positive psychology approach to work with individuals in a preventative manner. My research in this area will draw attention to an evidence-supported treatment alternative that needs to be part of the therapeutic conversation. As the knowledge of psilocybin-assisted therapy evolves and moves away from previous stigmatized understandings, therapists and policymakers can now shift towards how it is helpful and an innovative way to work with treatment-resistant individuals that have suffered in silence for too long.

Keywords: hallucinogens, psychedelics, psilocybin, psilocybin-assisted therapy, treatment-resistant disorders, depression, cancer, anxiety, substance use

Dedication and Acknowledgements

I would like to dedicate my capstone to my late mother Gayle Charlene Hildebrandt who passed away on March 13, 2021. She always supported me in following my dream to become a counsellor and would have been so proud to see me complete this program.

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Chapter 1

The use of psychedelic substances in a therapeutic setting is not a new idea. Traditionally, these substances have played a role in Indigenous cultures' ritualized healing and religious practices (Lieberman & Shalev, 2016). In the 1950s and 60s, researchers became interested in studying psychedelic substances to better understand the neurobiology of mental functioning and the therapeutic agents for mental disorders such as substance use, depression, personality disorders, and adjuncts to psychotherapy (Lieberman & Shalev, 2016). They were also studied by the Central Intelligence Agency (CIA) for more sinister purposes, such as brainwashing and prisoner interrogation (Lieberman & Shalev, 2016). Recreational usage of psychedelics in the late 1960s and their association with the anti-Vietnam War movement prompted the U.S. government to list them as a schedule 1 banned substance, considered to be unsafe and to have a high risk of abuse potential with no therapeutic indications (Lieberman & Shalev, 2016). In the past decade, there has been a resurgence of interest in psychedelic substances, particularly in the field of psychology (Lieberman & Shalev, 2016).

The purpose of this research is to review the literature involving full-dose psilocybin treatment as an adjunct to psychotherapy. The second purpose of this research is to review the applicability of psilocybin-assisted psychotherapy as a novel way of working with treatment-resistant disorders. The final purpose of this research is to make recommendations for the best practices of using psilocybin-assisted psychotherapy from a clinical perspective, along with recommendations for future directions in the research based on what I have discovered during the literature review section.

As the knowledge of psychedelic substances evolves and moves away from the stigmatized understanding of how they affect the human body and mind, the understanding can

shift towards how they are helpful instead of reinforcing the unfounded beliefs that led to criminalization.

“Recent studies have demonstrated that the degree of restriction for illegal drugs does not correlate with their risk of harm, and there is no formalized process for reviewing these determinations at the national or international level” (Lieberman & Shalev, 2016, p. 1199). As the growing research in this area continues to highlight the benefits of psychedelic substances, more progress can be made in the availability of funding for studies and the accessibility of psychedelic treatment options for those who suffer from treatment-resistant disorders.

In chapter one, I discuss the growing interest in psychedelic research, explain my connection to the topic, highlight the importance of psychedelic substances in working with treatment-resistant disorders, and define the key terms used in the paper.

Chapter two is a review of the psilocybin-assisted therapy literature. In this chapter, I clarify what is fact and what is fiction about psilocybin, outline the barriers that impact the research, and investigate how psilocybin can be used best when working with treatment-resistant disorders. I also focus on what is needed to utilize psilocybin safely, the different phases involved in psilocybin-assisted therapy, and the role of the therapist, music, and set and setting while in session. The last section summarizes the key findings in the areas of treatment-resistant depression, cancer-related disorders, and substance use disorders while also recognizing the limitations involved in psilocybin research.

Chapter three begins with a synthesis of the research discussed in chapter two, and the main themes that emerged are highlighted. Next reviewed is a section on what I believe the public would need to know regarding how psilocybin can be utilized in the treatment of currently undertreated mental health conditions. Finally, I conclude the paper with recommendations to

inform best practices when conducting psilocybin-assisted therapy in the clinical setting, and with recommendations for future directions of research in this area.

Why Psychedelic Research is Important

James Lake sees mental illness as the “pandemic of the 21st century” (Lake, 2017, p. 1), the next major worldwide health challenge. Currently, the majority of treatments available for psychopathological issues are heavily reliant on psychotropic medications, but according to Lake, “after decades of research and billions of dollars of industry funding, the evidence supporting pharmacologic treatments of major depressive disorder, bipolar disorder, and other psychiatric disorders is not compelling” (Lake, 2017, p. 1). The psychotropic medications being prescribed to clients are often accompanied by a list of side effects, many of which negatively impact the lives of those relying on the medication to lessen the symptomology associated with their disorders. “Many commonly prescribed psychotropic medications including antidepressants and antipsychotics are associated with serious adverse effects, including weight gain, increased risk of diabetes and heart disease, neurologic disorders, and sudden cardiac death” (Lake, 2017, p. 2).

Furthermore, Lake (2017) sees long-term usage of prescription medication with limited efficacy as leading to “long-term impaired functioning, work absenteeism, and losses in productivity” (Lake, 2017, p. 3). The rise in mental disorders contributes to the global burden of disease which has huge socio-economic costs but the research and development of psychopharmacology, the route of choice for most psychiatrist’s interventions, has been halted since 2010 (Schenberg, 2018). The US Food and Drug Administration’s (FDA) approval of new psychiatric molecular entities “fell from 13 in 1996 to one in 2016, with 49 approved between 1996 and 2006 and 22 from 2007 to 2016” (Schenberg, 2018, p. 1). According to Nutt et al.

(2020), “current medicines are derivatives of drugs discovered in the 1950s through serendipity and refined through pharmacological modifications” (p. 1). Even within the pharmacology field, innovation in the past ten years is slowing, meaning a further deficit in new ways to treat issues that continue to negatively impact the lives of those suffering from disorders.

Bickman (2008) speaks about the ineffectiveness and stagnation of mental health services. According to Bickman, treatment-as-usual (TAU) is treated as a commodity with little regard to its effectiveness or quality. Bickman brings attention to the limited monitoring of treatment effectiveness and recognizes that there is no financial incentive to deliver more effective treatment since compensation for mental health professionals is the same despite how successful they are with their clients. Bickman continues by pointing out that evidence-based treatments are rated on their efficacy within an experimental setting, which often is not the same environment as that utilized in the therapeutic setting.

Despite promising research in the area of psychedelic substances, many mental health professionals continue to distance themselves because of the persisting stigma that surrounds the subject matter. This reluctance to consider psychedelic therapy as a legitimate form of therapy continues to keep it on the fringe of the mental health services radar.

Personal Connection to Psychedelic Research

My relationship to this topic is one of interest rather than one of experience. I do not have firsthand experience with any of the psychedelic substances that are being looked at in this research.

My interest in this topic is also connected to the search for alternatives to the medications that are currently being used to treat anxiety, depression, terminal cancer, and substance use. I do not disagree that treatment using medication can be beneficial for some people, and I am not a

proponent of doing away with medication altogether. I do believe there is value in continually searching for more effective ways to treat these disorders. For me, this means searching for substances that have fewer negative side effects, less addictive properties, and less need to be taken daily. This is why I see promise in the research around the use of psychedelics, and specifically psilocybin.

I also feel strongly about the need to push past traditional ways of thinking that are no longer serving society in the way that they were once intended to. Seeing how quickly the public opinion on cannabis has changed as a result of legalization has been inspiring. I have witnessed people in my life that went from a stance of anti-cannabis to one of curiosity and interest in its ability to be used medically. Even if it did not change their opinion on whether they would ever use it, they were at least able to see why others would and do not view them in the same stigmatized way they once would have.

Just like cannabis is not for everyone, I believe that psychedelics and psilocybin are not for everyone either. That being said, as the collection of empirical evidence showing the efficacy of psilocybin treatment grows, I would like to see a similar attitude of acceptance develop. For those who are struggling with treatment-resistant disorders, having a publicly accepted alternative option that gives some much-desired relief from their persistent symptoms, could quite literally be lifesaving.

I am interested in seeing mental health services continue to grow and evolve to provide the best treatment possible. In the case of psychedelics, this means fighting an uphill battle to question the political decisions that made them schedule one banned substances and altering the public opinion about what psychedelics actually are. It is not an easy task but if it can ease the suffering for some, in my opinion, it is an option worth exploring.

Aside from researchers that are truly passionate about psychedelic substances, there does not seem to be much urgency within the mental health services to explore potentially revolutionary treatments. The current structures are set up in a way that is comfortable for those who have established positions within them. Supporting the movement that is pushing to reinstate schedule one substances could benefit clients suffering from undertreated mental health disorders, but it also lacks any noticeable benefit for those whose livelihood is intertwined with the current system. Real change happens when the rewards outweigh the risks, and until recently, maintaining the status quo has been more important than finding a way to help those who really need it.

From a personal standpoint, I understand why the re-emergence of psychedelic research has taken as long as it has to come back into focus. I grew up in a conservative, religious setting believing that all drugs were bad. The messages from my church, family, and society convinced me that drugs ruined people's lives, a far cry from the emerging ideas that they could be potentially helpful.

My perspective began to shift around the time that cannabis was being legalized for medical purposes. As the awareness of the health benefits of cannabis became more mainstream, and the research looking at the medicinal qualities of cannabis continued to grow, I began realizing how wrong the messages that demonized the use of cannabis were. Then I started to think about the possibility of psychedelics also being misunderstood. After reading Michael Pollan's book *How to Change Your Mind*, which described his research around the use of psychedelic substances to treat difficult conditions such as depression, addiction, and anxiety, my interest in this area was piqued.

Research using psychedelic substances has shown promising results with minimal side effects in areas that typically have been resistant to treatment. I saw this lack of side effects as an appealing benefit that demanded more attention. During my mom's fight with cancer, I observed the extensive side effects of the hydromorphone she was prescribed, in contrast to the medical cannabis options she used to treat the same pain. I could not help but think that more natural options should be available for those who are suffering. By exploring every possible option to find what works best, mental health services can offer their clients the most comprehensive services available.

Psychedelic Substances and Treatment-Resistant Disorders

The purpose of this research is to bring awareness to alternative ways of treating disorders that have been resistant to the current methods being used. The medications currently being used in treatment work to suppress the symptoms, whereas psychedelics address the underlying biopsychosocial causes. "Psychedelic therapy harnesses a therapeutic window opened up by the brain via the effects of the drugs to facilitate insight and emotional release and, with psychotherapeutic support, a subsequent healthy revision of outlook and lifestyle" (Nutt et al., 2020, p. 24). Nutt et al. see psychedelics working best with internalizing disorders by disrupting the rumination involved in the internal thoughts.

Having safe, legal environments to receive psychedelic treatments provides a much-needed legitimacy to the use of psychedelic substances. It's a way to shift the opinion of psychedelics from being viewed as recreational drugs to being viewed as plant medicines with the potential to positively change lives. Legitimate psychedelic treatments can challenge the negative and fearful view that these substances should be avoided and outlawed as they have been since the late 1960s.

Despite being on the list of schedule one banned substances, psychedelics are still being used outside of North America and in underground scenes within North America. By incorporating psychedelics into legitimate forms of therapy, it brings them into the mainstream of options available. It challenges the stigma attached to the use of plant medicine in a therapeutic setting both by therapists and potential clients. For those clients that continue to suffer from symptoms that are not being effectively addressed with TAU, psychedelic treatment programs offer the chance to try something new, something that has shown promising results in treating anxiety (Ross et al., 2016), depression (Nutt et al., 2020), cancer-related disorders (Ross et al., 2016), and substance use (Nutt et al., 2020).

Having competent full-dose psychedelic treatment plans available, and readily accessible, is a way to take the next step forward in a field that is desperate for progression. The current state of mental health services appears to be stagnant and in need of some fresh, new ideas. The services already in place are not prepared to adequately address the issues they are being confronted with. Innovation is needed and the work being done with psychedelics is showing promise for the future. As momentum continues to grow in this area, one of the next steps will be figuring out the most effective ways to safely harness the power of psychedelics in a therapeutic setting.

What the Literature Says

In an article looking at the therapeutic potential of plant-based psychedelics, such as psilocybin, Carhart-Harris and Goodwin (2017) note that they “have been used for hundreds if not thousands of years for holistic healing and there remains an active culture of self-medication with psychedelics for mental health” (p. 2106). Once the ‘War on Drugs’ began at the end of the 1960s, psychedelic research was discontinued, halting any further advances in the thinking and

practices of psychology and psychiatry in this area. However, countercultural groups continued to embrace the power of these substances which continue to impact society to this day (Carhart-Harris & Goodwin, 2017).

Why is there a recent push towards reviving the interest in the therapeutic use of psychedelics? In their paper titled *Psychedelic Psychiatry's Brave New World*, Nutt et al. (2020) discuss the factors that make a compelling argument for bringing psychedelic research back into the field of psychiatry. They reference the growing demand for addressing mental health concerns, the limited breakthroughs being made, the growing evidence of safety and efficacy, and the limited potential for abuse as key factors for the renewed interest. Nutt et al. also see the novel, rapid, enduring, and transdiagnostic action of psychedelic substances creating excitement and promise for the future in this area. Looking forward, Nutt et al. see the increasingly positive research results bridging the gap between psychotherapy and pharmacology, leading to more institutional support, and therefore more venture capital to continue to propel the movement forward. Unlike modern medications, psychedelic substances have a long history of use. Finding a way back to reliable substances that were once so widely used could be a breath of fresh air in a field that has grown stale (Nutt et al., 2020).

In an article written by Watts et al. (2017), they looked at the value individuals experiencing depression attached to their psilocybin treatment. Upon completion of the psilocybin treatment, the researchers observed a change in the subjects from feeling disconnected (from self, others, and the world) to feeling connected, and from avoiding emotion to accepting emotion. When they asked for a comparison between the psilocybin treatment and conventional treatments, patients reported that medications and some short-term talking therapies tended to reinforce feelings of disconnection and avoidance instead of connection and acceptance.

In an article exploring psychedelic-assisted psychotherapy, Reiff et al. (2020) looked at recent psilocybin trials that have proven effectiveness in treating anxiety disorders, substance use disorders, and end-of-life emotional suffering. They observed persistent antidepressant effects of psilocybin that lasted for weeks to months after several sessions. In opposition to current treatments, such as transcranial magnetic stimulation, that require multiple visits a week several times a month to show results, the use of psilocybin appears to be an attractive alternative (Reiff et al., 2020).

The new research that is coming out about the potential uses for psilocybin in a therapeutic setting seems to indicate an exciting and reassuring future for psychedelic treatments. It provides a spark of hope to both the practitioners and patients that have been longing for a new approach to work with palliative care patients and the debilitating, treatment-resistant symptoms associated with disorders like substance use, anxiety, and depression. As the field of psychology relearns what our forefathers already knew about the power of psilocybin, new innovative opportunities to capture its benefits in the therapeutic setting will arise.

Important Areas of Research

In the literature review portion of this research paper, I am focusing specifically on the use of a full dose of psilocybin in treatment for individuals struggling with anxiety, depression, terminal cancer, and substance use.

In the first section I outline the reasons why interest in exploring the usage of psilocybin in a therapeutic setting has started to regain popularity. The following sections are devoted to exploring the literature on the relationship between psilocybin and each disorder listed above.

There is also be a section focused on the importance of set, setting, and environment while administering psilocybin therapy.

The final section describes the different types of treatment programs that are currently available, how they implement the usage of a full dose of psilocybin into the program, and how successful they have been at treating each disorder.

Key Terms

- **anxiety disorder:** excessive worry and/or fear about future events that interfere with the normal day-to-day functioning of the individual experiencing it.
- **biopsychosocial:** the interrelation between biological, psychological, and social influences on the formation of a disorder.
- **dissolution of ego:** when the usual self-centred sense of self is replaced with an increased feeling of connection and union with others and the world.
- **efficacy:** the ability, especially of a medicine or a method of achieving something, to produce the intended result (Cambridge Dictionary, 2019).
- **major depressive disorder:** persistent feelings of sadness or loss of interest that interfere with the normal day-to-day functioning of the individuals experiencing it.
- **mental health services:** services used to diagnose and treat people with mental disorders; implements strategies to prevent mental disorders and ensures that primary healthcare workers can apply key psychosocial and behavioural science skills, such as interviewing, counselling, and interpersonal skills, to improve overall health outcomes in primary healthcare (“What Is Primary Care Mental Health?: WHO and Wonca Working Party on Mental Health,” 2008).
- **oceanic boundlessness:** refers to a mystical state of mind that involves feelings of insightfulness, bliss, unity, and spirituality.

- **plant medicine:** is a term that describes psychedelic substances used for healing purposes. Its purpose is to decipher the use of psychedelic substances from the use of recreational drugs.
- **psilocybin:** is a naturally occurring psychedelic compound produced in certain species of mushrooms that are often referred to as “magic mushrooms” (Wikipedia Contributors, 2018).
- **psychedelics substances:** substances that alter perception and mood and affect numerous cognitive processes (Nichols, 2016, p. 264). Examples include LSD, psilocybin, ayahuasca, mescaline, DMT.
- **psychopathology:** the study of mental disorders or behaviours that indicate psychological impairment.
- **psychopharmacology:** the study of the effects that drugs have on mood, sensation, thinking, and behaviour (Wikipedia Contributors, 2019).
- **psychotropic:** refers to drugs that alter the user’s mental state.
- **stagnation:** a situation in which something stays the same and does not grow and develop (Cambridge Dictionary, 2019).
- **stigmatization:** the act of treating someone or something unfairly by publicly disapproving of them (Cambridge Dictionary, 2019).
- **substance use disorder:** excessive use of substances (ex. alcohol, drugs) that interferes with the normal day-to-day functioning of the individual experiencing it.
- **symptomology:** signs, markers, or indicators of mental health disorders.
- **therapy-as-usual:** refers to the commonly accepted routine or usual methods of care used for particular disorders.
- **transdiagnostic:** refers to a treatment that can be similarly used across multiple diagnoses.

- **treatment-as-usual:** refers to the commonly accepted treatments used for particular disorders.
- **treatment-resistant disorders:** disorders that do not respond adequately or promptly to the usual methods of treatment for that disorder.

Chapter 2

Facts vs Fiction About Psilocybin

Psychedelic substances have a history of being misunderstood and misrepresented. The term hallucinogens, which is sometimes used interchangeably with psychedelics, is considered misleading since perceptual changes are only one feature of the psilocybin experience and perceptual changes at a normal dose rarely include hallucinations (Johnson et al., 2008). Johnson et al. acknowledge that ‘bad trips’ or overwhelming distress can occur and in extreme circumstances can result in dangerous behaviours. There is also the potential for prolonged psychoses triggered by the substances, but this is even less common (Johnson et al., 2008). Despite the above-listed possibilities and being listed as a Class A illegal substance, research has shown these substances to be relatively safe physiologically with a low risk of developing dependence (Johnson et al., 2008).

In this paper, the focus is on research involving full-dose psilocybin sessions. Microdosing is a practice that involves ingesting sub-hallucinogenic amounts of psychedelic substances as a way of capturing some of the benefits without experiencing the hallucinogenic effects (Anderson et al., 2019). Although there is an expanding online community of microdosers, the practice is still mainly recreational in nature and has only a minimal amount of formal research involving the subject (Anderson et al., 2019). For these reasons, the literature on full-dose psilocybin sessions is what is reviewed in this paper.

An article by Dolan (2021) focuses on a recent shift in the public’s perception of ‘magic mushrooms’ despite the rigid laws still in existence. According to Dolan, research has shown that harm, toxicity levels, and abuse potential are considered to be low and yet the drug still remains a banned substance.

The Dolan article (2021) documents the results of a study involving 151 participants in the US and Europe recruited from different websites and social media platforms reporting their perception of danger associated with ten different substances. Dolan notes that most participants considered psilocybin to be relatively safe compared to the other listed substances, especially participants with prior psilocybin experience. Even non-users considered psilocybin to be less dangerous than heroin, cocaine, prescription pain killers, GHB (date rape drug), ecstasy, tobacco, and alcohol (Dolan, 2021).

The findings of this study suggest that the public's perception of whether psilocybin should be considered dangerous is more aligned with the scientific data than the legal drug classification systems (Dolan, 2021). Although the subjects of this study were self-selected, the results do indicate a transformation in the way the public feels about psilocybin, how it's used, and whether or not it should remain an illegal substance.

Barriers of Psilocybin Use

Research in the area of psychedelics substances continues to gain momentum and promising findings continue to accumulate but there is still a noticeable resistance that acts as a barrier to the availability and legitimacy of psychedelic treatment options.

Bogenschutz (2016) lists some possible reasons why psilocybin is struggling to gain acceptance such as small, uncontrolled samples with unreplicated results that trivialize the legitimacy of psilocybin-assisted treatments. He also recognizes the difficulty of shedding the stigma attached to substances with a reputation of being dangerous, addictive, risky, and illegal.

Bogenschutz (2016) sites the suspicion around the mediators of change as an obstacle to acceptance. He explains how a substance that induces unusual, non-rational, and ineffable

experiences as a means of treatment is difficult for those in the behavioural sciences to digest as a valid option.

Finally, Bogenschutz (2016) touches on the problematic piece around finances and why psilocybin is not considered an attractive investment for industry funding. Since psilocybin is a naturally occurring substance that takes a minimal amount of doses to generate change, the ability for corporations to profit is limited making it less attractive than other medications to produce and market (Bogenschutz, 2016). With mild interest from private industry, the search for support falls on governments, and change in this area has been slow over time.

With these barriers in mind, it has taken time to shift the momentum in the area of psilocybin research. It has been an uphill battle for psychedelic researchers and others to re-establish psilocybin as a legitimate option not just for future research but for adjuncts to current treatment. As the barriers continue to be identified and addressed the needed changes are taking place in a way that shows a brighter future for psilocybin-assisted therapy.

How Psilocybin Works

Psilocybin is a naturally occurring tryptamine found in *Psilocybe Mexicana* Heim and other species of psychoactive mushrooms that have historically been used by different native cultures for shamanic and/or spiritual rituals (Brown et al., 2017). Historically, Indigenous cultures have viewed hallucinogens as plants and fungi of divine descent which were taboo to use outside of specific circumstances (Johnson et al., 2008). Psilocybin experiences are often described as psychedelic and/or hallucinogenic due to the distinct impact they have on the consciousness of the user (Brown et al., 2017). “The effects have been characterized as an intense dream-like state with colorful visual illusions, changes in auditory, tactile, olfactory,

gustatory, and kinesthetic perceptions, altered perceptions of time and space, changes in body image and sensations, and intense mood changes” (Brown et al., 2017, p. 1544).

The psilocybin effects generally peak 90 minutes after ingestion and usually subside and resolve four to six hours after (Tai et al., 2021). Modern research has found that psilocybin can “increase optimism, psychological wellbeing, trait openness, and life satisfaction in an enduring way following just a single dose in healthy populations” (Lyons & Carhart-Harris, 2018, p. 2).

In a study involving psychedelic treatments, Brekke et al. (2020) observed: “alterations of conscious states, as well as a wide range of psychological, cognitive, emotional, and biological effects that may be relevant for their therapeutic action, when administered within a (psycho) therapeutic context” (Brekke et al., 2020, p. 926). While conducting a systematic review of the different psychedelic treatments, Brekke et al. found evidence that these subjective experiences included the relevant factors needed for the therapeutic effect to take place.

In a study conducted by Mason et al. (2020), they looked specifically at the role of regional alterations in glutamate and how they affect ego dissolution in psilocybin sessions. This research is based on the understanding that psychedelic substances can induce profound alterations in consciousness such as transient and dose-dependent distortions in how individuals experience a sense of self (Mason et al., 2020). The dissolution of the ego is characterized by a reduction in self-referential awareness and disruption to the usual boundaries between self and the world leading to increased feelings of unity (Mason et al., 2020).

There is also emerging evidence from other research that classic psychedelic substances (LSD, psilocybin, DMT) stimulate the serotonin receptors located on the cortical pyramidal neurons, which are the suspected mechanisms of action for the hallucinogenic effects (Mason et

al., 2020). Research indicates an emphasized role of the glutamate system in the serotonin receptor-mediated effects on brain function and behaviour (Mason et al., 2020). Activation of the serotonin receptors leads to a glutamate-dependent increase in the activity of pyramidal neurons in the prefrontal cortex while subsequently modulating prefrontal network activity (Mason et al., 2020). The increase in extracellular glutamate has been suggested to activate the AMPA receptors on the same neurons and this leads to an increased expression of brain-derived neurotrophic factor (BDNF), a protein implicated in neuronal survival and growth that occurs less frequently in pathological populations (Mason et al., 2020). Vollenweider and Kometer (2010, as cited in Mason et al., 2020) suggest that serotonin receptor-mediated glutamate release is the final common pathway for acute actions of psychedelics, and the underlying mechanism of therapeutic effects.

After psilocybin is ingested it rapidly dephosphorylates into psilocin which is believed to be responsible for the psychoactive effects that accompany the use of psilocybin (Brown et al., 2017). The binding and partial agonist activity at serotonin 5-HT_{2A} receptors are required for the psychoactive effects to be produced from the psilocin (Brown et al., 2017).

SSRIs and psilocybin both work by modulating the central nervous system serotonin levels. Psilocybin directly activates the 5-HT_{2A} receptors on the prefrontal cortical neurons (McCorvy, 2016). Elevated cortical 5-HT_{2A} receptor expression is linked to depression-related suicide and SSRIs are reported to reduce cortical 5-HT_{2A} receptor expression via receptor down-regulation (McCorvy, 2016). In contrast to SSRIs, psilocybin is suspected to possess sustained antidepressant effects after only one use by downregulating serotonin receptors, but more research is still needed (McCorvy, 2016). It is also thought that psilocybin acts on more

than just the 5-HT_{2A} receptor and the unique effect is due to a combination of actions happening on other receptors at the same time (McCorvy, 2016).

Studies suggest that the mystical experiences that take place during psilocybin sessions might be integral to the antidepressant process. A single dose is often enough to ignite a long-term reduction in depressive and anxiety symptoms making it an attractive alternative front-line treatment, especially for populations that are actively suicidal or terminally ill, and time is of the essence (McCorvy, 2016).

The psilocybin experience has empirical support for promoting psychotherapeutic change by accepting and moving through challenging emotions while under the influence of the substance (Kaelen et al., 2018). “One key difference between psychedelic therapy and other forms of psychotherapy (and conventional pharmacotherapy) may be the capacity of psychedelics and music to rapidly facilitate deeply felt and personally meaningful emotionality” (Kaelen et al., 2018, p. 517).

Kaelen et al.’s (2018) findings illuminate the importance of preparation before the sessions commence. They see an increased openness in the individual as key in permitting the music to evoke a positive experience in the patient through a state of surrender and curious engagement with therapeutic content that emerges. Therapeutic benefits may stem from the combination of the substance and how it interacts with the music (Kaelen et al., 2018).

Mood disorders are associated with increased negative affect, reduced positive affect, and hypersensitivity to negatively biased information (Barrett et al., 2020). Negative affect is also the core component of the cycle of addiction with symptoms such as cravings, withdrawal, preoccupation, anticipation, and re-administration of drugs (Barrett et al., 2020). Looking more

specifically at depression there seems to be an elevated amygdala reactivity to negative affective stimuli (Barrett et al., 2020).

Dysfunction in the amygdala and anterior cingulate cortex (ACC) have both been implicated in substance use disorders and have been implicated in supporting aberrant negative affect in these disorders (Barrett et al., 2020). Psychedelics are effective when working with mood disorders because of their ability to acutely reduce the processing of negative affective stimuli while also increasing positive mood (Barrett et al., 2020).

Functional magnetic resonance imaging (fMRI) studies support the idea that psilocybin reduces amygdala activity and connectivity while viewing negative facial expressions and decreases activity in the ACC during the resting state and autobiographical memory recall (Barrett et al., 2020).

Mertens et al. (2020) also looked at the therapeutic mechanisms of psilocybin. The study examined the neural mechanisms responsible for the changes in the amygdala section of the brain in response to the ingestion of psilocybin (Mertens et al., 2020). The researchers predicted that the post-psilocybin changes would likely occur in the frontal cortex while the TRD subjects performed the same emotional face paradigm task that was given to solidify a baseline measure at the beginning of the study. They also predicted decreased functional connectivity (FC) between the amygdala and the ventromedial prefrontal cortex (vmPFC) during the emotional face task. The vmPFC is an important component for emotional processing that has top-down inhibitory effects on the limbic regions and is implicated in emotional control, inhibition, and regulation (Mertens et al., 2020). Mertens et al. hypothesized that the reduction of FC between the vmPFC and the amygdala would explain the increased amygdala responsivity after ingesting psilocybin. Also, the alteration of the FC that takes place between the amygdala and the vmPFC

could be related to the post-treatment changes in depression severity and rumination tendencies observed in TRD patients. The researchers had a particular interest in rumination since it is known as a vulnerability factor in the development and maintenance of depressive episodes and has been found to have different neural underpinnings for depressed patients than healthy ones (Mertens et al., 2020).

The Mertens et al. (2020) study was focused on the changes in the brain FC after 19 TRD patients who underwent two psilocybin-assisted therapy sessions one week apart. Of the 19 participants, 17 were classified with severe/very severe depression with an average of 17.7 years with the diagnosis. They had tried 4.6 different antidepressant medications and had tried at least one form of psychotherapy. The study included a single four-hour preparation session, support during the two-dose sessions, and an integration session that followed the therapeutic dose (Mertens et al., 2020).

Mertens et al. (2020) found some support for the key hypothesis of psilocybin creating an altered FC between the amygdala and the prefrontal cortex. They also observed a reduction in the vmPFC FC to the right amygdala during the face processing task, especially when viewing fearful and neutral faces. These results could imply a decreased inhibitory input from the vmPFC to the right amygdala which could influence the amygdala's responses (Mertens et al., 2020). The FC between the vmPFC and the right amygdala post-treatment was also significantly related to rumination levels in the patients at the one-week post-treatment mark and the three-month mark (Mertens et al., 2020). The lower the connectivity the less rumination they observed.

The researchers saw these results as important in understanding how decreased amygdala-prefrontal connectivity post psilocybin session are mechanisms for symptom improvement in TRD patients (Mertens et al., 2020). They also found that vmPFC showed

significantly higher FC with areas of the visual cortex during the face processing task and were also linked to changes in depression and anxiety scores at one-week post-session. This change in visual cortex activity and the connectivity between the vmPFC and amygdala could be the result of increased task engagement, changes in emotional stimulus recognition, and processing post-treatment (Mertens et al., 2020).

A potential explanation for the results found in Mertens et al.'s (2020) study is that antidepressants and psilocybin have fundamentally different actions on emotional processing. Antidepressants work by downregulating emotional responsiveness and psychedelics allow patients to fully engage with their emotions (Mertens et al., 2020). These explanations fit well with Mertens et al.'s (2020) findings that increased amygdala responsiveness and decreased engagement of prefrontal control regions could be the drivers involved in increasing the ability of TRD patients to reconnect emotionally post psilocybin treatment.

The Mertens et al. study (2020) shows that psilocybin should be considered a novel and promising treatment for TRD and other disorders. The results provide further understanding as to which mechanisms are involved in the changes observed after using psilocybin in treatment, and how these changes increase the patients' ability and willingness to engage with their emotions post psilocybin therapy. Although more research in this area is needed, the findings also provide some evidence that increased amygdala responsiveness and decreased FC to the prefrontal control regions may be related to the increase in sensitivity and acceptance post-treatment (Mertens et al., 2020). The results further illuminate the idea that psilocybin shows promising results with TRD patients because the mechanisms of change targeted by psilocybin may be different than traditional antidepressant medications that have shown limited success with this population of patients.

In a study by Barrett et al. (2020), alteration of emotions and brain function in response to psilocybin usage was explored. The researchers looked at the long-term, enduring impact of psilocybin on negative affective stimuli using 12 volunteers in an open-label pilot study. The study included assessments one day before the 25 mg psilocybin dose and then one week and one month after the dosage. The researchers used a battery of self-report state and trait affect measures completed at the different assessment periods, as well as fMRIs conducted for baseline measures and after emotional processing tasks.

Barrett et al. (2020) found a decrease in negative affect and a decrease in amygdala responses to emotional stimuli. They also reported an increased response to reward-learning, increased attention to decision-making circuits, increased responses in somatosensory and fusiform gyros during high-demand emotional conflict tasks, and global increases in functional connectivity. These effects were still considered significant even one month after the psilocybin dosage (Barrett et al., 2020).

These results are indicative of a neuroplastic period where neural processing of affective stimuli is altered. Psilocybin administration leads to a shift in absorption that causes an increase in extroversion and openness, and a decrease in neuroticism (Barrett et al., 2020). The results of this study suggest that psilocybin leads to a shift in affect and neural correlates of affective processing that continues to endure long-term. This reduction in negative affect works against the rumination process that is responsible for maintaining mood disorders and could also be responsible for psychological and neural changes that have antidepressant effects (Barrett et al., 2020).

The findings of this study also suggest a disruption of negative components like cravings and withdrawal symptoms associated with substance use disorders (Barrett et al., 2020). At the

one-month follow-up, negative affect and brain responses seemed to rebound back suggesting that psilocybin initiated a dynamic and neuroplastic change that lasted for at least several weeks (Barrett et al., 2020). There were also findings that strong functional connectivity across networks may reflect a domain-general cortical plasticity process that leads to the same changes in the affective processing observed in Ly et al.'s (2018, as cited in Barrett et al., 2020) findings highlighting the pre-clinical evidence for the psychoplastogenic properties of psychedelic substances. These results speak to the lasting effect of a single dose of psilocybin compared to pharmaceutical interventions that sometimes take up to three weeks before effects are experienced.

Meikle et al. (2019) described the different findings on which mechanisms of action are involved in psilocybin-assisted therapy. Findings from the Carhart-Harris et al. (2017, as cited in Meikle et al., 2019) study suggest that a 'reset' mechanism is associated with the decrease in functional connectivity within the default mode network (DMN); a network that is associated with introspection, self-reference, and auto-biological memory. Psychedelics have also been shown to increase synchrony between the high-order functions and the low-order, task-positive network structures that are not usually correlated (Meikle et al., 2019). Alonso et al. (2015, as cited in Meikle et al., 2019) saw the changes that take place as a rebalancing of predictive processing and a reduction in excessive top-down processing resulting in less cognitive and affective bias. This rebalancing can positively alter participants' ability to forecast future events, decrease self-focus, and increase perceptual coupling which potentially interrupts the abstract self-oriented rumination involved in depressive thinking (Meikle et al., 2019).

The way that psilocybin works is thought to be different than how antidepressants and ketamine work (Shelton & Hendricks, 2016). Although ketamine and psilocybin are both

associated with mystical experiences linked to improvements in depression and anxiety, psilocybin is noted for its ability to produce long-lasting results (Shelton & Hendricks, 2016). The benefits of psilocybin also include the ability to see lasting results after a single dosage, therefore relieving patients from the stress of having to take daily doses to continue to see results (Shelton & Hendricks, 2016). There is also a push for the use of psilocybin from a positive psychology perspective to confront the universal feelings associated with the fear of death in otherwise healthy individuals (Shelton & Hendricks, 2016).

In contrast to the usual antidepressant medications that induce change gradually, psilocybin works more acutely and intensely to increase neuroplasticity and alter functional connectivity in a single session (Meikle et al., 2019). Meikle et al. see these functions as creating a window of opportunity for psychotherapy to guide and solidify the changes that are observed in post-psilocybin sessions. These changes in functional connectivity suggest that psilocybin could help treat a wide range of mental disorders that specifically involve deeply entrenched, maladaptive patterns of thinking, feeling, and behaving. Meikle et al. see the potential for reintroducing psilocybin as a novel treatment in several areas that have historically been under-treated as progressive. Even if it is not approved as a stand-alone treatment, work can be done between researchers and authorities to develop the proper framework for psilocybin-assisted therapy to be considered as an exciting alternative to the current medications in use (Meikle et al., 2019).

Breeksema et al. (2020) were able to highlight the important mechanisms of the psilocybin experience that contribute to a meaningful and impactful experience. They include gaining insight, altered self-perception, increased feelings of connectedness, transcendental experiences, and an expanded emotional spectrum. Breeksema et al. also recognized that

multiple mechanisms could be acting simultaneously in producing therapeutic outcomes that are relevant to what is being targeted in treatment. Insight and altered self-perception are often related to increased feelings of self-love, self-worth, and self-compassion, whereas ego-dissolution, and spiritual and/or mystical aspects of healing are noticed in treating substance disorders (Breeksema et al., 2020).

Interconnectedness is a common feature in psilocybin research. Psychedelics can intensify emotions and ignite a greater range of emotional reactivity which allows participants to process deep emotions, release unresolved or inaccessible emotions, and experience emotional breakthroughs leading to long-term positive changes (Breeksema et al., 2020). In other studies, patients specifically attributed the long-term effects to their ability to overcome the difficult experiences faced while under the influence of psilocybin (Breeksema et al., 2020). An improvement in symptoms was not the only benefit reported by subjects. Some subjects saw the reduction of symptoms as palling in comparison to the more profound benefits related to an added feeling of overall well-being (Breeksma et al., 2020).

The changes observed in response to psychedelic compounds further develop the understanding of how the neural network supports a well-delineated sense of self and other through antidepressant and/or anxiolytic mechanisms of action (Summergrad, 2016). Neuroimaging studies have suggested changes in the coupling of the posterior cingulate cortex and medial prefrontal cortex and the coupling of the medial temporal lobe and neocortex (Summergrad, 2016).

What makes psilocybin unique is its ability to treat disorders in a way that other currently used methods do not. Through the mystical-type experiences brought on by psilocybin, there is an alteration to the conscious state that allows for the dissolution of the ego and an increased

ability to accept and move through challenging emotions. The neuroplasticity that results from the activation and downregulation of the serotonin receptors allows for more synchrony between the high and low order functions. The ability to rebalance the default responses resulting from rumination with what is sometimes referred to as a brain 'reset' is a main reason why using a full dose of psilocybin has shown success with treatment-resistant disorders (Meikle et al., 2019). Psilocybin is also gaining momentum because of its long-lasting effects in areas that historically have relied upon the use of pharmacological treatments. No medication currently available in psychiatry has such pronounced and lasting effects with as little as one or two discrete exposures (Bogenschutz, 2016).

A Brief History of Psilocybin Research

Original research in the area of psychedelics was performed by the US Army using what they referred to as hallucinogens as interrogation agents on nonconsenting subjects while paying little attention to the set and setting of the experiments resulting in more adverse reactions than modern research (Johnson et al., 2008). The next wave of research paid more attention to preparation and interpersonal support and the results reflected experiences that were more positively valued (Johnson et al., 2008).

The adverse effects of psychedelics were the focus of the anti-drug movement in the late 1960s and early 70s causing research in this area to fall out of favour. Contributing to this change was the growing popularity of recreational psychedelic usage, as well as Timothy Leary's irresponsible advocacy for hallucinogen use by youth which undermined an objective approach to studying them (Johnson et al., 2008). The negative publicity that he received resulted in a sharp decline in the funding available for new research and eventually to a loss of interest in psychedelics as a whole (Johnson et al., 2008).

A renewed interest came again in the late 90s following new brain imaging techniques and neuropharmacological findings recognizing the potential in treating acute psychosis (Johnson et al., 2008). The early studies did not pay much attention to control conditions or groups in the way that recent research does, but they still managed to see favourable results for cancer patients suffering from anxiety and depression (Johnson et al., 2008).

Interest in psilocybin has also been piqued following new research about its safety and efficacy (Brown et al., 2017). Grob et al. (2011, as cited in Brown et al., 2017) suggest that with effective preparation and appropriate dosing conditions psilocybin can be used to alleviate existential anxiety and depression associated with terminal illness often with only a single dose. This symptom reduction leads to improvement in the patient's condition for months after (Brown et al., 2017).

Important Features for a Safe and Impactful Psilocybin Experience

The push to list psilocybin as a schedule one banned substance was based on anecdotal evidence of adverse psychological experiences reported by individuals partaking in recreational settings. As research on the topic expands it is becoming clear that set and setting are important factors to be taken into account when using psychedelics in a therapeutic setting. The risk associated with psilocybin, and other psychedelics, is uniquely not physiological but rather psychological in nature (Johnson et al., 2008). Hallucinogens are not typically considered addictive nor are they associated with a withdrawal syndrome, meaning they are low risk for administering to human subjects (Johnson et al., 2008).

The use of psilocybin in treatment is not without physiological or psychological risks, however minimal, making screening and preparation of the individual before consumption of the substance imperative. Prioritizing safety in psilocybin sessions sets the stage for a deeply

meaningful and spiritual experience (Johnson et al., 2008). Throughout history, psychedelics have been used in many ways, some more ethical than others. During this time themes such as setting up safeguards, structuring the use, and restricting the use to environments that are guided and show respect for the substance have emerged as principles for best practices (Johnson et al., 2008).

Careful consideration is taken when selecting subjects for psilocybin research because of the potential psychological risk of having a ‘bad trip’ which involves feelings of anxiety, fear/panic, dysphoria, and paranoia (Johnson et al., 2008). Psilocybin is recognized as an amplifier of feelings, so if a subject is not properly prepared there is the risk of the experience taking a negative turn. There have been situations where psychedelic usage has resulted in prolonged psychosis, but it has been explained as a catalyst of an earlier onset for a psychotic break that would have inevitably happened at a later point for the individual (Johnson et al., 2008). There has also been concern over ‘flashbacks’ or hallucinogen persisting perception disorder (HPPD) which according to the literature is quite uncommon and when it is experienced it is not often described as a negative experience but rather a benign and even a pleasurable one (Johnson et al., 2008).

Ensuring safety begins by selecting physically healthy volunteers with no family history of psychotic disorders who are not pregnant or currently taking certain medications, like antidepressants (Johnson et al., 2008). Individuals with elevated traits of rigidity or emotional lability are more likely to have negative experiences while under the influence of psychedelics and therefore are not a safe choice of subjects for research in this area (Johnson et al., 2008).

However, since the Johnson et al. study in 2008, there has been an abundance of research suggesting that psychedelics can be used safely and successfully to treat psychiatric disorders

such as treatment-resistant depression, anxiety, and substance use. Johnson et al. did acknowledge that studies targeting disordered populations would involve different considerations and may involve making special exceptions with additional safety measures. For example, “in a study of hallucinogen-assisted therapy for depression or anxiety, individuals should be excluded whose symptoms of depression or anxiety are sufficiently severe to warrant immediate treatment with medication (e.g. due to suicidal ideation)” (Johnson et al., 2008, p. 609).

More recent research focused on treatment-resistant populations has involved extra considerations around medications and proper preparation to guard against negative psilocybin experiences. For example, to be included in most studies participants are asked to temporarily suspend the use of medications “to avoid the confounding effects and potential interactions of concurrent antidepressant use” (Davis et al., 2020, p. 482). Pre-psilocybin sessions are also included in the design of studies involving treatment-resistant populations to properly prepare individuals with elevated traits of rigidity and emotional lability in order to lessen the possibility of a negative experience (Tai et al., 2021).

In an open-label study looking at how psilocybin enters, moves through, and leaves the body, Brown et al. (2017) gave sequentially escalating doses of psilocybin to 12 healthy adults. The results suggest that a dose of 0.3 mg/kg seemed to be the ideal amount to use with patients. When exposed to doses of 0.6 mg/kg, which far exceeds the likely dosage in any therapeutic setting, the researchers did not find any serious physical or psychological events at the time of the study or 30 days after the study (Brown et al., 2017). These results show that even large doses of psilocybin pose little risk to the subjects as long as they are properly screened. Although this study was completed with healthy volunteers, similar studies involving treatment-resistant

participants showed consistent findings. When participants are properly prepared and not at risk for psychosis, large doses of psilocybin do not appear to be a cause for concern.

Role of Therapist

Tai et al. (2021) discuss the importance of proper training for the therapists that are involved in the psilocybin session and what the important factors are to consider during the sessions. Safety is one of the main considerations for psilocybin-assisted therapy since approval from regulators, review boards, and ethics committees is required for permission to conduct any research and/or therapy (Tai et al., 2021).

Part of the training for therapists conducting psilocybin-assisted therapy is learning how increased attentional mobility, introspection, and problem-solving can bring about increased awareness of personal goals (Tai et al., 2021). Tai et al. recognized the importance of being patient-centred and non-directive to allow participants to construct their own potential solutions to any incompatible goals. A skillful psilocybin-assisted therapist works to engage all aspects of the client's experience while staying within their window of tolerance to work productively and safely through self-directed inquiry and experiential processing (Tai et al., 2021). The therapist can have a beneficial effect by encouraging the participant to direct their attention inwards and look at things from a different and sometimes more helpful perspective (Tai et al., 2021). This practice can increase internal psychological flexibility, introspection, and problem-solving ability (Tai et al., 2021). It can also involve raising awareness and evaluation of the biological, social, and psychological variables occurring within the participant's body and how they can be involved in gaining valuable insight and facilitating change (Tai et al., 2021).

Special attention is given to the therapeutic alliance during treatment since according to Brekke et al.'s research (2020) it can help the patients surrender and overcome intense

emotionally challenging experiences that arise during the psilocybin session. Furthermore, the alliance with the therapists provides the security that is crucial for having a ‘safe trip’ while under the influence of psilocybin.

As for the necessary training needed for therapists to be psilocybin guides, Tai et al. (2021) start with the need for the practitioner to hold a professional license in good standing. They also state the importance of having instructors who are considered ‘experts through experience’ draw upon personal experiences as patients of psilocybin-assisted therapy in a way that is helpful for their students (Tai et al., 2021). The therapists must have clinical experience in at least four different psilocybin research studies before leading sessions independently (Tai et al., 2021).

Tai et al. (2021) also encourage the use of mentorship between experienced and inexperienced therapists involving discussion, clinical scenarios, and lessons that can be learned together while supporting participants of a study. Webinars that address the emerging questions that may come up for therapists in training is another way that Tai et al. list as proper training to become a qualified therapist in psilocybin sessions. Fidelity scales are used to assess the consistency of therapists ensuring that they are working safely in session with participants (Tai et al., 2021). Much like any other type of therapy, ethics and cultural sensitivity are also important aspects to consider while administering psilocybin-assisted therapy (Tai et al., 2021).

Phases of Psilocybin-Assisted Therapy

Psilocybin-assisted therapy is usually broken down into three phases: preparation, ingestion, and integration (Tai et al., 2021). From the therapist’s perspective preparation involves building an alliance with the participants through genuine curiosity and forming a trusting bond by being present and focused on the participant (Tai et al., 2021). During the preparation phase,

the therapist focuses on expanding the participant's threshold for navigating through potentially distressing periods during the psilocybin session (Tai et al., 2021). Preparation meetings to review consent and explain the logistics of the study should be done in the same room as the administration session as a way to familiarize the participant with the space (Johnson et al., 2008). Collecting background information is a way to build rapport while learning important details about the participant's life that may surface during the session (Johnson et al., 2008).

The next step is to explain the possible range of experiences the participant could expect during the session. These include physical sensations, perceptual changes, alteration of emotions, and thoughts, feelings, or insights concerning their personal history (Johnson et al., 2008). Pre-emptive guidance for handling any difficult hallucinogenic experiences is also provided. This discussion may include instructions on how to mentally surrender and trust that they will return to their usual experience of consciousness when the substance wears off (Johnson et al., 2008).

Roseman et al. (2018) noted the importance of preparing participants in advance of the psilocybin session. Working with participants to facilitate trust and build rapport set the stage for a meaningful experience to take place (Roseman et al., 2018). It is important to help shift the participant's mindset to one that is available for emotional openness and free from the psychological resistance that curtails progress from being made during the experience (Roseman et al., 2018).

In the psilocybin phase, Tai et al. (2021) described a focus on safety and working with the participant to ensure that any distress that arises in session does not become overwhelming. They recommend promoting an attitude that is courageous, trusting, and open so that they can experience everything available to them. Tai et al. view the benefit of the therapists themselves

having gone through the psilocybin experience so that they can empathize with what the participant is going through.

When it comes to administering the dosage, Johnson et al. (2008) once again state the importance of safety by suggesting that a physician is available to address acute hypertension if the participant's blood pressure becomes dangerously elevated. They also encourage the two monitors to be vigilant for signs of psychological distress and stay close to the participant should they need to use the washroom or stand up and walk around while under the influence of the substance. One monitor should always be present with the participant throughout the duration of the session (Johnson et al., 2008).

It is imperative to have at least one therapist present to compassionately address any issues involving disoriented participants wanting to leave the study site while under the influence of psilocybin (Johnson et al., 2008). The ability of the therapist to stay calm and in control is essential for 'talking down' the client should they experience any adverse reaction during their session. (Johnson et al., 2008). Johnson et al. suggest supporting touch and verbal reminders as effective ways to reassure a disoriented participant. They believe that if the participants have been adequately screened, prepared, and guided, that reassurance from a compassionate and empathetic monitor should be enough to diffuse psychological distress in the vast majority of cases.

Johnson et al. (2008) support the use of eyeshades and headphones to listen to pre-selected, supportive music as a way to feel safe and to avoid any added distractions from environmental stimuli or social pressure to interact with the monitors sitting in the room. They also suggest waiting until after the drug effects have worn off before engaging in any in-depth

discussion about what is happening for the participant and to encourage them to ‘collect experiences’ rather than verbalize them as they are happening.

The purpose of the final phase of integration is to give the participant a chance to reflect on their journey and gain insight into what it meant for them (Tai et al., 2021). The goal is to support the participant in connecting with a full range of emotions and the cognitive and physical experiences present in the psilocybin session and find the best way to integrate them into their own personal narratives (Tai et al., 2021). In a post-psychedelic session, Johnson et al. (2008) encourage the practice of handing off the participant to a friend or family member (or stay overnight on-site) so they do not have to drive or be responsible for any other potentially dangerous activities while recovering from the experience. For added feelings of safety, they recommend that the monitors also provide the participants with their contact information to use if they need any further support following the session.

Johnson et al. (2008) also recognized the importance of follow-up sessions to monitor any lasting effects and to provide an opportunity for debriefing about any thoughts or feelings that may have come up while reflecting on the psilocybin experience. The monitors likely have a better understanding of what the participants went through than other people in their lives because of their experience, training, and familiarity with altered states of consciousness.

Set and Setting

Set and setting have been found to play an important role in the psychedelic experience. Brekke et al. (2020) observed enduring and clinically significant improvements in treatment-resistant patients that received the placebo instead of the psychedelic compound. They see these effects as a testament to the importance placed on the extra-pharmacological factors such as trust, rapport, attention, length of treatment, and the treatment setting used in the studies.

To help create positive rapport the psilocybin-assisted therapy monitors, and other involved staff, should be friendly, welcoming, compassionate, sensitive, and curious about the participant's well-being (Johnson et al., 2008). Knowing that the mood of the participants plays a key role in the direction their psilocybin experience goes, it is important to give extra consideration to how they are treated pre-session. Johnson et al. (2008) pointed out the importance of having knowledgeable monitors with a distinguished ability to connect with the participants. Recognizing what is happening for the participants while in the altered state helps the monitors relate to the spiritual issues that can come up during mystical-like experiences (Johnson et al., 2008). Monitors with experience using breathing techniques, yoga, meditation, and mindfulness can be effective in assisting the participant along their journey (Johnson et al., 2008). Johnson et al. see the ability to be sensitive, empathic, and respectful in a clinical setting as paramount. Having multiple monitors (preferably of the same gender as the participant) present during the session is another way to ensure an added feeling of safety and security for the participant (Johnson et al., 2008).

Russ et al. (2019) looked particularly at the importance of participant's mental state when engaging in a psilocybin session. The occurrence of a mystical experience as a predicting factor for the patient having a positive outcome is something that has been found in numerous studies (Russ et al., 2019). The presence of a mystical experience was predictive of favourable long-term outcomes and antidepressant effects in clinically depressed patients (Russ et al., 2019).

The Russ et al. (2019) study drew its sample from a crowdfunded population of individuals who had recently self-administered psilocybin. The researchers acquired detailed written responses to open-ended questions before asking the participants to complete scaled questions investigating their state of mind. They were interested in looking at traits like

absorption and openness before and after the session and participants' perceptions of their own long-term changes of self and well-being (Russ et al., 2019). Because of the atypical way that Russ et al. collected their data, any conclusions from the study were meant to inform possible ways to deliver optimal conditions to participants in the future and not to draw any firm conclusions.

Russ and colleagues (2019) found that mental states of surrender or preoccupation at the time of ingestion can explain the variance in mystical or adverse psilocybin experiences that are related to long-term positive change. These results suggest that when providing support for individuals in psilocybin therapy it would be beneficial to pay special attention to the mental state of the participant before administering the substance (Russ et al., 2019).

Russ et al. (2019) also recognized that absorption, spiritual motivation, openness, and surrender were the strongest predictors of whether the individuals had a mystical-like experience, and apprehension and deservingness tended to interfere with the ability to have a mystical experience. Russ et al. observed that mystical experiences were associated with other positive changes like feelings of gratitude, joy, trust, empathy, social concern, and with lower scores on negative measures like anxiety, fear, and impatience. These observations once again point to the importance of the individual's mental state before participating in psilocybin therapy and the importance of appropriate preparation and understanding of what to expect during a psilocybin session.

The physical setting is another key consideration. Johnson et al. (2008) emphasized the importance of creating an interpersonal space that is conducive to positivity. They suggest constructing a setting that is aesthetically pleasing and not overly clinical in appearance as a way to avoid any acute psychological distress. They recommend a setting that is comfortable,

relaxing, and physically safe. Décor that may be disorienting or frightening while under the influence of psychedelics should be avoided (Johnson et al., 2008). The absence of phones is endorsed to avoid distraction, or the alarming feeling should it ring during the session (Johnson et al., 2008). There should also be a private washroom to avoid any interaction with strangers during the session (Johnson et al., 2008). Roseman et al. (2018) recommend creating an open and welcoming environment with dimmed lights, shaded eyes, calm emotionally focused music, and support from an empathetic and knowledgeable therapist.

Careful, considerate, and detailed planning sets the participants up for the best chance at success. With the right mindset and a calm, supportive environment, they can focus on navigating their way through what many describe as one of the most meaningful, memorable, and life-changing experiences of their life (Agin-Liebes et al., 2020).

Russ et al. (2019) recognized that most psilocybin research participants studied in a controlled environment show favourable results. It is in uncontrolled environments where adverse experiences such as fear, anxiety, and paranoia may occur more frequently (Russ et al., 2019). The amplitude of response to psilocybin is related to dosage, particular personality traits, the mental state or ‘set’ at the time of ingestion, and the characteristics of the setting during ingestion (Russ et al., 2019).

Set and setting are also the focus of Hartogsohn’s study (2016). Both set and setting are important when using psychedelics since the effects of the substances are highly dependent on nonpharmacological factors, like expectation, preparation, intent, and the social environment they are taken in (Hartogsohn, 2016).

Other research looking at similar phenomena found that placebo effects contribute almost twice as much as the therapeutic effects of antidepressant medications (Hartogsohn, 2016). A

‘positive approach’ in general-practice consultation raised patients' improvement rates 25% and post-myocardial infarction patients who did not take their placebo medication regularly were twice as likely to die than those who did (Hartogsohn, 2016).

The expectations of the individual are a key part of the placebo effect. Benedetti (1996, as cited in Hartogsohn, 2016) and Vicker (1996, as cited in Hartogsohn, 2016) found that patients that did not know they were receiving treatment showed dramatically lower placebo-related improvement rates. It has even been found in some studies that patient’s expectations can change or reverse the effects of active pharmaceutical agents (Hartogsohn, 2016). Social interaction alone can create a placebo effect. Whitehorn and Betz (1960, as cited in Hartogsohn, 2016) observed that different personalities of doctors were seen to be responsible for differing results in standard treatment used with schizophrenia patients.

Set and setting in the field of psychedelics has historically been misunderstood. Set and setting are terms introduced by long-time psychedelic advocate Timothy Leary and his colleagues (1963, as cited in Hartogsohn, 2016). They hypothesized that psychedelic substances acted like a magnifying glass for consciousness. It does not change what exists in the mind but rather augments it (Hartogsohn, 2016). Leary et al. (1963, as cited in Hartogsohn, 2016) saw the importance of personality, preparation, expectations, and intent along with environmental factors such as physical, social, and cultural surroundings during the experiments as being of top importance to see positive results. Similarly, Hyde (1960, as cited in Hartogsohn, 2016) found that patients taking LSD in a group, rather than alone, experienced fewer negative effects highlighting the importance of environmental factors for positive psychedelic experiences. Leary’s way of thinking lined up well with the wide array of results from LSD studies during the

1960s since the sensitivity to set and setting provided in each study varied vastly (Hartogsohn, 2016).

In Hartogsohn's study (2016) they looked at how the placebo effect and set and setting involve meaning, whether it is in the context of a doctor's office or a shamanic ritual. Moerman and Jonas (2002, as cited in Hartogsohn, 2016) see the meaning that we attach to pills, doctors, and symbols of medical treatment as responsible for the placebo responses that exert both positive and negative effects on health. After the resurgence of psychedelic therapy, researchers have made a stronger effort to properly prepare subjects using music, flowers, pictures, and strategies that involve positive interactions between the participant and therapist (Hartogsohn, 2016).

“If placebo response is understood as meaning response, and if psychedelics magnify the perception of meaning it may be that psychedelics augment meaning response” (Hartogsohn, 2016, p. 1263). Hartogsohn sees this as a way to explain how successful healing is associated with ritualistic and other meaningful settings. Participants in psychedelic studies typically rate their experience as being one of the most influential, meaningful, and spiritually significant experiences of their lives (Hartogsohn, 2016). This knowledge allows for the integration of placebo effects and set and setting into psilocybin studies as a way to empower the clients to take a more active role in the process of healing (Hartogsohn, 2016). Hartogsohn also sees this as a way to empower practitioners by providing additional tools to enhance and optimize their chances of making successful progress with their clients.

Breeksema et al. (2020) suggest that set and setting are almost as important as the pharmacological factors when implementing psilocybin-assisted treatment. Studies that involved significant preparation before the treatment such as establishing trust, rapport, and attention in a

safe setting showed patient improvement whether they were in the placebo or active drug group (Breeksema et al., 2020). These findings suggest that it can be hard to discriminate between the contextual and the drug effects, implying that both are of importance (Breeksema et al., 2020).

Role of Music in the Psilocybin Experience

While reviewing the literature, music arose as an important factor in psilocybin treatment. Music is seen as a way to support the patients non-verbally while conducting psychedelic therapy (Kaelen et al., 2018). Studies have shown that psychedelics significantly modulate music-evoked emotion and imagery while simultaneously sparking feelings of personal meaningfulness related to the music (Kaelen et al., 2018).

The importance of music in the psilocybin experience was explored by Kaelen et al. (2018). They used semi-structured interviews with 19 patients that had undergone psilocybin therapy for treatment-resistant depression to learn about how welcomed and unwelcomed music influenced the patients' experience. All the patients in this study listened to the same music to avoid any confounding variables. Kaelen et al. (2018) chose music that was mainly contemporary music such as ambient, neoclassical, and traditional/ethnic music as a way to minimize religious association and support mystical experiences within a secular framework. The playlist used in the study was specifically designed to mimic the psilocybin experience (pre-onset/onset/building towards peak/peak/re-entry/return).

Kaelen et al. (2018) found that music was associated with the occurrence of 'mystical experiences' and 'insightfulness'. The most frequently reported themes were that the music intensified the experience and produced mental imagery during the process. The results showed the music as providing guidance, grounding, and helped carry the listener to psychologically different places (Kaelen et al., 2018). They found that the nature of the musical experience

significantly predicted the reduction of depression one week after ingesting psilocybin whereas the intensity of the drug did not. These findings suggest that the substance is not working in isolation, but as an interaction between the substance and the subjective experience of the music that promotes positive therapeutic outcomes (Kaelen et al., 2018). When the music matched up with the patients' intrinsic emotional state it increased their openness to the experience, and when it did not resonate it diminished the experience (Kaelen et al., 2018). The enhanced receptivity to music may activate emotions, thoughts, and memories that are personally salient, and the music can guide the experience in ways that are therapeutically significant (Kaelen et al., 2018). The findings in this study suggest that music plays a central role in psilocybin-assisted therapy (Kaelen et al., 2018).

The effects of psilocybin are well-established but as a mechanism of change, the impact of the substance alone is not responsible for the success that it has seen in the research. Set and setting are important considerations when administering psilocybin-assisted therapy. This includes properly screening the participants and selecting the size of the dose based on sound research. It also involves trained therapists that are knowledgeable on the use of psilocybin in the therapeutic setting and have themselves been involved in similar psilocybin experiences.

Working through the different stages of psilocybin-assisted therapy include properly preparing the participants by building rapport and setting expectations, being available to the participants as a guide through the experience and following up with the participants to establish what the experience meant to them at the time and what it means for them moving forward. The mindset, the physical setting, and the music work simultaneously to provide the best opportunity for a meaningful psilocybin experience capable of having a long-lasting positive impact on the condition of the participants.

Growing Interest in Psilocybin

There seems to be a growing consensus that new treatment options that rely on novel mechanisms of action are needed in the area of mental health since the focus on the monoamine reuptake inhibitors has shown limited results to this point (Meikle et al., 2019). Psilocybin is a substance that has gained attention due to the mechanisms of action involved in its antidepressant qualities and the relatively low side effects burden (Meikle et al., 2019).

According to Williams and Warner (2019, as cited in Meikle et al., 2019), psilocybin-assisted therapy has been designated by the US Food and Drug Administration (USFDA) as a breakthrough therapy in depression. The push to expedite the production of prescription psilocybin for treatment purposes comes as a result of studies like Bonomo et al.'s (2019, as cited in Meikle et al., 2019) that confirm its low risk for potential harm to the user, its beneficial mood effects, and its ability to alleviate affective and addictive disorders (Meikle et al., 2019). The novel effects are of particular interest to the treatment-resistant population who fail to respond to conventional antidepressants and are desperately looking for new options.

Drug research in the area of treatment-resistant disorders continues to lack innovation. Many of the new treatment ideas are mix and match versions of current pharmacological treatments with the hope of finding a combination that works. One reason for this lack of progress is because drug discovery is a high-risk and expensive business, with a lot of failures before any breakthroughs are made (James et al., 2019). Areas of unmet need occur when the healthcare system cannot afford the high prices needed to produce new medications (James et al., 2019).

'Emerging from the Dark Side' is an article by James et al. (2019) that discusses the positive outcomes of psilocybin-assisted psychotherapy studies. They suggest these new results

could have a positive effect on the treatment-resistant community as a whole and could help psilocybin emerge from the ‘Dark Side’ and become a component of mainstream western medicine (James et al., 2019).

Psilocybin-assisted therapy has shown benefits related to positive psychology; a way to intervene before a mental illness is diagnosed (James et al., 2019). James et al. also suggested that there is evidence of public support for the availability of psilocybin in healthcare systems from the university-educated population and those in favour of the mainstream scientific perspective. This shift follows the growing understanding that the banning of psychedelic substances curtails important research and does nothing to stop or reduce consumption (James et al., 2019). Furthermore, there is a growing understanding that substances like tobacco and alcohol go unabated despite being responsible for more morbidity and mortality than all other illicit products combined (James et al., 2019). As perspectives change on which substances are actually dangerous, a better understanding of psilocybin and its potential to contribute to the field of mental health can develop.

Treatment-Resistant Disorders

Treatment-resistant (TR) disorders are in a class of their own. TR disorders do not respond in the same way to TAU and need treatment alternatives since the first-line methods do not have the desired or expected results (Bhui, 2017). “The term often applied dispassionately, medically, and devoid of empathy is ‘treatment resistance’, meaning that they do not benefit from or respond to medication, psychotherapy, electroconvulsive therapy (ECT), or even new neuromodulatory treatments”. (Bhui, 2017, p. 443). Although there is a lack of consensus of what exactly the definition of treatment-resistance should be, the term generally refers to the failure of front-line treatments to effectively treat the disorder.

According to Bhui (2017), TR disorders are often missed because tools like suicide assessments overlook the contextual information that encapsulates the true experience of the patients. Bhui recognizes how ineffective methods of identifying TR disorders restrict opportunities for early intervention. An example that Bhui gives is that depression in parents is associated with mood dysregulation in offspring. Knowing this to be the case, early intervention could be a way to intervene before a TR disorder can develop. To avoid TR and chronicity of disorders, Bhui says clinicians need to be better informed so they can work with this population using first-line interventions with a higher rate of success than the ones currently available.

The chronicity of mood and anxiety disorders are associated with higher healthcare usage, lower socio-economic functioning, reduced work productivity, and lower quality of life when compared to the more acute forms of these disorders (Vollbehr et al., 2018).

Major Depressive Disorder and Treatment-Resistant Depression

Despite substantial advances in treatment and management strategies for depression, less than 50% of patients respond to first-line antidepressant treatment or psychotherapy (van Bronswijk et al., 2019). In van Bronswijk et al.'s meta-analysis, they found evidence to support the inclusion of psychotherapy as an add-on to pharmacological and neurostimulatory treatments for patients experiencing treatment-resistant depression (TRD). Bronswijk et al. see the addition of psychotherapy to TAU as a justified way to provide a better treatment outcome for the TRD population, one that has been historically difficult to treat.

TRD is associated with a longer duration, increased severity, greater impairment, and a higher risk to the public and to the diagnosed individual (Erritzoe, 2018). TRD is often characterized as a marked impairment that is not only a burden on the individual but also their families and the healthcare system (van Bronswijk et al., 2019). Clinical reviews show that most

of the research on treatment for TRD is in the area of pharmacology or somatic treatments and there is still relatively little research about the use of psychotherapy as an adjunct to treatment (van Bronswijk et al., 2019).

According to the WHO statistics (2017, as cited in Heuschkel & Kuypers, 2020) across age, gender, sex, and nationality approximately 4.4% of the global population is affected by major depressive disorder (MDD). Symptoms of MDD include depressed mood, anhedonia, fatigue, feelings of worthlessness, guilt, suicidal ideation, agitation, executive deficits, as well as changes in appetite, weight, and psychomotor functions (DSM-5, 2013, as cited in Heuschkel & Kuypers, 2020).

Nolen-Hoeksema (2017, as cited in Heuschkel & Kuypers, 2020) describes MDD as a complex interplay of psychological and biological factors that create negative thinking patterns due to deficiencies on emotional, cognitive, and social levels. These thinking patterns in combination with inadequate emotional regulation and excessive rumination are how the depressed mood is maintained over an extended period (Heuschkel & Kuypers, 2020). Depressed individuals have rigid ways of thinking, less dispositional empathy, higher distress, and underdeveloped communication skills (Heuschkel & Kuypers, 2020). They excessively seek approval and negative feedback to confirm the negative self-images they have of themselves (Heuschkel & Kuypers, 2020).

Feelings of social isolation are common since poor social skills and self-centred introversion can provoke conflict in social situations and act as an added stressor that further perpetuates depressive symptoms (Heuschkel & Kuypers, 2020). It has also been found that neuroplasticity is impaired in individuals with MDD meaning that their brain is unable to functionally adapt in ways that healthy individuals can (Heuschkel & Kuypers, 2020). In place of

neuroplasticity, the brains of individuals with MDD demonstrate hyper-connectivity with the default mode network (DMN) which is the area of the brain that is activated during rumination (Heuschkel & Kuypers, 2020). Heuschkel and Kuypers also suggest that MDD is associated with dysregulation within the hypothalamic-pituitary-adrenal (HPA) axis which is a part of the neuroendocrine system that regulates stress and immune responses. Increased secretions of cortisol and impaired negative feedback loops result in chronically elevated levels of cortisol. This leads to an increased vulnerability to stressors, causes disruption in the immune systems, and ultimately promotes the emergence of depressive symptoms (Heuschkel & Kuypers, 2020).

Depression is a leading cause of disability, and for those experiencing depression the relative risk of all-cause mortality is 1.7 times greater than the general public (Davis et al., 2020). There are several pharmaceutical options for treatment, but they lack efficacy, are accompanied by adverse side effects, and because they need to be taken consistently, they are associated with adherence difficulties (Davis et al., 2020). These side-effects include “weight gain, drowsiness, diabetes, tremors, and severe effects if the person suddenly stops treatment” (Bright & Williams, 2018, p. 468). Pharmaceutical treatments do result in reduced or remitted symptoms for some patients, but approximately 30-50% of patients do not respond fully and 10-30% are considered treatment-resistant (Davis et al., 2020).

Current First-Line Treatment for MDD and TRD

The need for reform in major depressive disorder (MDD) treatment is clear when research on the topic is closely examined. According to Ruberto et al. (2020), over a third of patients with MDD do not respond in an adequate way to the first-line treatments currently being used and are therefore considered treatment-resistant. Ruberto et al. acknowledge that TRD patients have a more severe course of illness and an increased risk of suicide.

The next step in treatment is to switch antidepressant medications, augment the medications, or switch to a different medication. Ruberto et al. (2020) recognize the ambiguity around the decision of which path to follow, the lack of consistency, and the varied success rates. The literature finds little evidence that switching to another medication in the antidepressant class is effective as a second line of treatment (Voineskos et al., 2020). Treatments such as ketamine and esketamine are showing themselves to be superior options and appear to be among the most effective (Ruberto et al., 2020). Also, augmentation with second-generation antipsychotic medications, like quetiapine or aripiprazole, is preferred over switching to alternative antidepressant medications (Ruberto et al., 2020). The combination of dantrolene and fluoxetine is another approved treatment, but its use is limited due to the metabolic side effects (Ruberto et al., 2020).

Although there are a number of treatment strategies in place to deal with TRD, there does not seem to be one strategy that is efficacious and widely accepted. Deciding which strategy is best depends on the unique set of benefits and drawbacks as well as the tolerability and response time for each patient (Ruberto et al., 2020). Ruberto et al. recognize that decisions on the best course of treatment are shared between the patient and the clinician since many important factors need to be considered, such as time to respond when working with an individual that is actively suicidal. Patients are commonly put in positions where they are forced to sacrifice tolerability for faster action (Ruberto et al., 2020).

Electroconvulsive therapy (ECT) is another technique used to treat TRD. ECT uses high-frequency electrical pulses to the non-dominant right hemisphere and vertex for unilateral ECT, or bitemporally for bilateral ECT, two to three times a week, for six to 18 sessions (Voineskos et al., 2020). Despite being recognized as the best option for TRD, it lacks popularity because of

the invasiveness of the procedure, the association with memory loss, and the restricted access to the therapy (Voineskos et al., 2020).

Another direction in TRD treatment involves the use of anti-inflammatories since c-reactive proteins and cytokines appear to be elevated in patients with MDD, and more specifically TRD (Voineskos et al., 2020). Research in this area has shown that anti-inflammatory therapy may have a novel role in treating TRD patients (Voineskos et al., 2020).

Cognitive-behavioural therapy (CBT) is the most widely used psychotherapeutic treatment for MDD based on the understanding that depressed individuals struggle with cognitive-negative biases involving unrealistic negative perspectives of themselves and the world (Lyons & Carhart-Harris, 2018). MDD patients tend to see the future as bleak and often over-predict negative results in unknown future events. This tendency is accompanied by more “dysfunctional attitudes, feelings of hopelessness, negative thoughts, and pessimism than healthy individuals” (Lyons & Carhart-Harris, 2018, p. 2).

Other non-traditional methods such as hatha yoga have been explored as ways to treat treatment-resistant mood and anxiety disorders because of research findings that it can help lessen psychological distress and help disrupt repetitive negative thinking, (Vollbehr et al., 2018). However, Vollbehr et al. did not show it to be as effective as TAU, although it was shown to reduce depression more than psychoeducation alone.

Psilocybin-Assisted Treatment for MDD and TRD

Psilocybin treatment is unique because it affects the serotonergic and glutamatergic systems, has a lower risk for addiction and toxic effects, and is not associated with long-term perceptual, cognitive, or neurological dysfunction (Davis et al., 2020). Davis et al. chose to look

at the use of psilocybin for its antidepressant qualities that have rapid and sustained effects on mood and cognition and its potential to “improve or save lives” (p. 2).

Psilocybin is thought to be helpful for individuals with MDD and TRD since the serotonin 2A receptors are expressed most abundantly in the default mode network (DMN) regions which are linked to trait pessimism and neuroticism, both contributing factors to depression (Lyons & Carhart-Harris, 2018). Insufficient signaling to the serotonin 2A receptor may result in inflexible thinking so increasing the signal as psilocybin does, can ‘lubricate the mind’ and provide an opportunity for new ways of learning (Lyons & Carhart-Harris, 2018). Psilocybin-assisted therapy is well tolerated and has impactful results with TRD patients (Lyons & Carhart-Harris, 2018).

In their 2018 study, Lyons and Carhart-Harris investigated the degree of pessimism and depressive bias present in TRD affected individuals and the ability of psilocybin to treat them. It is an open-label pilot study with a mixed-model design measuring depressive symptoms in TRD participants and comparing them with a group of healthy non-treated control participants that are matched in age, gender, and education. The researchers administered a test dose and a therapeutic dose to the TRD patients a week apart.

The results from the study showed that after treatment TRD patients did show a shift towards a more positive view of future events which allowed them to make more accurate predictions about their future, similar to the healthy control participants (Lyons & Carhart-Harris, 2018). In other words, the TRD patients were more pessimistic at baseline but this bias disappeared after the psilocybin sessions (Lyons & Carhart-Harris, 2018). Many of the patients from this study had enduring improvements that persisted up to half a year later, similar to results seen in research done by Griffith et al. (2008, as cited in Lyons & Carhart-Harris, 2018),

MacLean et al. (2011, as cited in Lyons & Carhart-Harris, 2018), and Carhart-Harris et al. (2016a, as cited in Lyons & Carhart-Harris, 2018).

Davis et al.'s study (2020) looked at 27 pre-screened, MDD diagnosed individuals that were not currently using antidepressant medication. The participants were randomly assigned to either the immediate or the delayed treatment group. The intervention period of this study included at least 18 in-person visits over eight weeks that also included two psilocybin administration sessions with follow-up meetings after each (Davis et al., 2020).

The results of the Davis et al. study (2020) documented rapid and enduring antidepressant effects following psilocybin-assisted therapy with MDD patients. The effect sizes of the study were two and a half times greater than those found in psychotherapy and four times greater than the effect seen in psychopharmacological treatments (Davis et al., 2020). The results were similar to those found when using ketamine, except that the effects were more substantial and longer-lasting (two days to two weeks vs four weeks).

Similar to the studies referenced by Davis et al., psilocybin was viewed as having a low potential for addiction and minimal adverse effects (Davis et al., 2020). Davis et al. see their psilocybin-assisted therapy results as generalizable beyond MDD since the involved mechanisms of change could be transdiagnostic in nature and could be helpful for substance use disorders, cancer patients, and even healthy volunteers (Davis et al., 2020).

In an article written by Bright and Williams (2018) the subject of psychedelic-assisted psychotherapy and whether or not it has a future in the field of mental health was explored. They speak specifically to treatment-refractory or treatment-resistant disorders that do not respond to the current first-line treatments that are widely accepted as best practices.

Bright and Williams (2018) push for psychiatrists to re-examine their beliefs on the safety of psychedelic-assisted therapy due to the growing acceptance of psychedelic substances, like psilocybin, as safe interventions when used in a clinical setting. As the research on psychedelic substances continues to grow and the long-held beliefs about the danger of ingesting these substances evolve, psychologists, policymakers, and ethics committees will be under pressure to adjust the beliefs they currently harbor (Bright & Williams, 2018). If the goal is to provide the best help available for clients, psychedelic substances like psilocybin deserve to be included in the conversation, especially for those individuals with TR symptoms that continue to be under-serviced by TAU.

Watts et al. (2017) looked at the connection between psilocybin experiences and feelings of increased connectedness in individuals being treated for depression. They had 20 patients enroll in an open-label trial of psilocybin for TR depression and collected their data from a six-month follow-up using a semi-structured interview. The study included screening, preparation, dosage, and follow-up sessions.

Watts et al. (2017) found that 15 out of 20 participants showed some degree of reduction in depressive symptoms at the six-month follow-up session. Of the 15 with reduced symptoms, seven showed a 50 % reduction and six showed remission in their symptoms (Watts et al., 2017). In contrast to the results from the Agin-Liebes et al. (2020) study that showed results strengthening over time, Watts et al. (2017) found that the average treatment results were large for the first five weeks but declined to the levels of conventional treatment after three to six months. That being said, most patients in the Watts et al. (2017) study still felt discernable benefits after six months and reported a preference for psilocybin over traditional treatments.

Speaking directly to the potential concerns of psychedelics substances, Watts et al. (2017) did not observe any craving behaviour that would suggest that psilocybin had any addictive qualities, nor did they have any reports of psychoses or persisting hallucinations. What they did find was that patients experienced less rigid ways of thinking that allowed for an acceptance of painful memories and a lasting improvement of their condition, an ideal starting point to begin talk therapy. Patients were able to switch from feeling disconnected to connected and from avoidance to acceptance which differed from the medications and talk therapies they had engaged in that perpetuated disconnection and avoidance (Watts et al., 2017). From the results they collected, the researchers believed that psilocybin works in a paradigmatically novel way that is different from other interventions (Watts et al., 2017). Future research should seek clarity on how exactly it works for patients and if it's an approach that should be used more consistently with treatment-resistant disorders.

In another study centred around treatment-resistant depression (TRD), Erritzoe et al. (2018) focused on the effects of psilocybin on personality. The study looked at 20 TRD patients in an open-label feasibility study. The researchers' inclusion criteria allowed moderate to severe unipolar major depression that had not shown any improvement despite undergoing two courses of pharmacologically distinct antidepressant medication for a minimum of six weeks (Erritzoe et al., 2018). Of the 20 participants, five patients had previously used psychedelics and four had used them in a recreational setting. Also, 17 of the participants had previously undergone psychological therapy/counselling (Erritzoe et al., 2018). The study consisted of one preparation session and two psilocybin sessions a week apart. The researchers had the participants come back one day and one week after the second psilocybin session to examine the process of integrating their experience.

Erritzoe et al. (2018) found that the clinical improvement observed in the patients was associated with significant changes in the personality measures. The researchers noticed a significant drop in the neuroticism scores, an increase in openness and extraversion, an upward trend in conscientiousness, and no change in agreeableness.

These are important findings for the population living with depression. Until this study was completed all the research in this area has focused on healthy volunteers. The observed increase in participant openness to action and values associated with the psilocybin experience is significant for individuals that typically feel isolated and depressed. Psilocybin-assisted therapy provides an active and encouraging approach for individuals to shed their self-centred ways of thinking to get outside of their own minds and consider the values and worldviews of others (Erritzoe et al., 2018).

For the participants, the changes occurred quickly and had lasting results (Erritzoe et al., 2018). This observation challenges long-held beliefs that slow, subtle, gradual personality changes are the expectation when treating depression (Erritzoe et al., 2018). The data from this study showed changes that happened much more rapidly than what has been observed in other therapeutic interventions (Erritzoe et al., 2018). Miller (2004, as cited in Erritzoe et al., 2018) referred to this as 'quantum change'. Erritzoe et al. recognized that participants that had a greater spiritual experience also showed an increased level of extraversion. They suggest that the enduring impact observed in psychedelic therapy is linked to the profound insights that participants experienced during the spiritual journey.

I think this study is iconic in its ability to show first-hand the impact that psilocybin therapy has not just on healthy subjects, but on subjects that have been struggling for a long time with ineffective treatments for depressive disorder. Such significant findings have potentially

life-altering implications for individuals that have experienced a lack of hope for effective treatment given the current therapeutic options available. Such results allow researchers to question what they know to be possible and therefore can lead to more efficacious treatments for a population desperate for relief

The Heuschkel and Kuypers literature review (2020) looks in-depth at the effects of mindfulness meditation (MM) and psilocybin on MDD-related factors. They found that MM and psilocybin are both novel treatments with promising efficacy. Separate they were effective but when combined they were even more so. The researchers found that MM and psilocybin worked in similar ways and had similar effects on mood, social skills, and neuroplasticity, but different effects on the body's executive functions, neural core networks, and neuroendocrine and neuroimmune systems. The effect on mood was dose-dependent for both MM and psilocybin and the neuroplastic changes were more pronounced with psilocybin after a single dose but took more sessions for MM (Heuschkel & Kuypers, 2020). They found that the combination of MM and psilocybin was clearly beneficial for all measures except for executive functions.

MM mental strategies incited change in emotional and cognitive self-regulation long-term (Heuschkel & Kuypers, 2020). Psilocybin was found to have neuromodulatory effects that helped the brain achieve a sense of flexible cognition that allowed for personal insights to assist in diminishing negative biases (Heuschkel & Kuypers, 2020). The combination of MM and psilocybin shifts the mind and the thought patterns in a more positive direction where the individuals can achieve a more open-minded outlook, gain control over strong emotions, and improve their ability to communicate effectively while under the influence of psilocybin (Heuschkel & Kuypers, 2020). As indicated by Heuschkel and Kuypers, the combination of the

two may also enhance psychological factors like mood control and relationship satisfaction that are often lacking in individuals with MDD.

Another important element that came up in Heuschkel and Kuypers's review (2020) was the role of psilocybin-induced ego dissolution that occurs during a MM session that could be a key reason for the endurance of positive changes in psychosocial functioning (Heuschkel & Kuypers, 2020). MM adjusts the prefrontal and limbic activity, as well as HPA reactivity, through top-down control (Heuschkel & Kuypers, 2020). Psilocybin promotes global network disintegration and anti-inflammatory effects using transient bottom-up processes (Heuschkel & Kuypers, 2020). So, when the two are used in conjunction there is a two-way reorganization of neural networks that helps rumination, and the down-regulation of neuroendocrine and neuroinflammatory responses (Heuschkel & Kuypers, 2020).

The results of the Heuschkel and Kuypers study (2020) show the ability of psilocybin to effectively treat MDD by targeting the main symptoms and addressing the issues in ways that antidepressant medication cannot. MM can be used as a second approach that works in a different way to help the MDD symptoms. The combination of the two treatments provides a non-intrusive, competent, and medication-free alternative for treating MDD.

In a study looking at the quality of acute psychedelic experiences, Roseman et al. (2018) administered the altered state of consciousness questionnaire (ASC) with 20 TRD diagnosed participants after two doses of psilocybin. The researchers used measures such as oceanic boundlessness (OBN) and dread of ego dissolution (DED) to understand whether the participant faced any mystical-type or challenging experiences during their sessions. Roseman et al. relied on self-reported information collected five weeks after the second psilocybin session.

Roseman et al. (2018) discovered that psilocybin produced an elevated level of OBN and a dampened level of DED in the participants that predicted the long-term clinical outcomes they experienced. The OBN levels were significantly more predictive of a positive outcome than hallucinogenic and mind-revealing qualities like visual and auditory perceptions (Roseman et al., 2018). Roseman et al. also found that a higher experience of DED was connected to less positive clinical outcomes. These findings suggest that the therapeutically significant effects are closely linked to the experiences that participants engage in while under the influence of psilocybin (Roseman et al., 2018). This suggestion parallels Jokela et al.'s study (2007, as cited in Roseman et al., 2018) which found that phenotypic expression of 5-HT_{2A}R genotypes is dependent on the influence of environmental factors, and Carhart-Harris and Nutt's study (2017, as cited in Roseman et al., 2018) that showed enhanced sensitivity to context is an important function of 5-HT_{2A}R receptor signaling.

The results of the Roseman et al. study (2018) indicate that there are good reasons for considering psilocybin-assisted treatment for TRD individuals. They also imply that multiple factors are at play when positive results are observed in psilocybin research. One factor that stands out as important is the quality of the experience that the individual has while under the influence of psilocybin and the meaning it has for them (Roseman et al., 2018).

Pokorny et al. (2017) looked at the effect of psilocybin on empathy and moral decision-making. Impaired empathetic abilities are a common denominator for psychiatric disorders like MDD (Pokorny et al., 2017). There is also evidence that a higher number of episodes in MDD patients is associated with a greater reduction in perspective-taking abilities (Pokorny et al., 2017). Empathetic abilities may become increasingly impaired as the mental illness progresses and this is seen as a contributing factor in severe cases of depression (Pokorny et al., 2017).

Pokorny et al. (2017) hypothesized that when faced with moral decisions individuals with MDD would be more likely to respond in a utilitarian fashion where the outcome justifies the means. Such responses are seen as a failure to conform to the social norms to protect others and are associated with antisocial behaviour (Pokorny et al., 2017). This predicted increase in utilitarian responses in reaction to personal moral dilemmas has been observed in patients with alcohol and polysubstance dependence (Pokorny et al., 2017). There is growing evidence in the literature suggesting that psilocybin enhances positive mood and lessens the processing of negative emotions, which is what Pokorny et al. wanted to test in their study.

The Pokorny et al. study (2017) included 32 healthy participants recruited from local universities. Participants were asked to refrain from using illicit psychoactive drugs two weeks before their first session and individuals who should not ingest psilocybin for health reasons were screened out. The Pokorny et al. study was a double-blind, randomized, placebo-controlled, within-subject design with two experimental sessions involving a moral dilemma task (MDT) 160 minutes after the psilocybin had been administered and an altered state of consciousness assessment.

Pokorny et al. (2017) reported that psilocybin had distinct effects on the social cognition of the subjects by enhancing social cognition but not moral behaviour. The results from this study agree with other studies that psilocybin likely promotes emotional empathy by activating the 5-HT_{2A/1A} receptors suggesting that these are the receptors that should be targeted when treating individuals with dysfunctional social cognition, such as individuals with MDD or TRD.

The use of psilocybin-assisted therapy in the field of MDD and TRD has shown promising results. Psilocybin ‘expands the mind’ and is thought to open up new and positive pathways in the brain to combat rigid, dysfunctional, and neurotic ways of thinking. Disrupting

the connection between the vmPFC, amygdala, and PFC allows for less rumination and more freedom to address problematic issues. Increased neuroplasticity leads to more flexible cognition and an improved ability to communicate and feel more connected and conscientious. When individuals experiencing TRD feel less stuck they are better able to adopt a less self-centred perspective to get out of their own head, dissolve their ego, and show more emotional empathy when considering the values and worldviews of others. The mystical-like experiences that often accompany the psilocybin experience involve a spiritual journey that provides insight into the problems participants are facing and encourages the search for meaning and solutions to their problems. Furthermore, psilocybin is faster acting, longer-lasting, and is accompanied by fewer side effects than antidepressants. These features make psilocybin-assisted therapy an appealing option for individuals struggling with TRD.

Psilocybin for Cancer-Related Disorders

Cancer is among the leading causes of death worldwide (Shelton & Hendricks, 2016). Accompanying a cancer diagnosis can be a prevalence of depression and anxiety which are often under-treated as a result of the cancer treatment being prioritized (Shelton and Hendricks, 2016). When it comes to assessing the efficacy of current treatments for cancer-related depression and anxiety results are limited because of the scarcity of treatment options. Life-threatening or terminal illnesses are often accompanied by substantial stressors for both the diagnosed individual and their families (McCorvy, 2016). These stressors are compounded by the existential crises associated with impending death and can often be expressed through depressive and anxiety symptoms (McCorvy, 2016).

Patterson and Van Ameringen (2016) looked at what the standard first-line treatments are for treating anxiety. According to them, antidepressant medications like selective serotonin

reuptake inhibitors (SSRIs) and cognitive-behavioural therapy (CBT) are the first efforts for treatment. Bandelow et al. (2008, as cited in Patterson & Van Ameringen, 2016) found that responses to this kind of treatment are less than optimal, with between 40-60% of patients still suffering residual anxiety symptoms. Furthermore, Patterson and Van Ameringen point out that research on how to treat those who do not respond to first-line treatment is limited, leaving many clinicians to seek guidance from refractory depression literature with limited success. There has been no drug approved to help treatment-resistant (TR) anxiety which leaves clinicians in a position where they use mix and matching strategies like SRI augmentations with other classes of agents, or with CBT to find answers for the patients (Patterson & Van Ameringen, 2016).

While looking at the limited evidence from TR anxiety studies it becomes clear that the current treatment strategies in place are not working like they should (Patterson & Van Ameringen, 2016). Patterson and Van Ameringen found a modest effect in the reduction in symptom severity when using the augmentation strategies and no significant differences were found for changes in functional impairment. They also found that there was a high rate of placebo effect in their study, which has often been a problem in anxiety disorder treatments. The findings of this study do not support pharmacological augmentation as a next step treatment for TR anxiety patients since it does not show evidence of improving functionality or treatment response (Patterson & Van Ameringen, 2016).

This is a problem that is unique to TR anxiety patients since there are many different options of monotherapeutic agents available for treatment (Patterson & Van Ameringen, 2016). With this in mind, the advances that have been made for using psilocybin-assisted therapy to treat TR anxiety are a glimmer of hope for those who have been suffering silently.

The unsatisfying therapeutic options currently available to terminally ill patients have left the door open for more efficacious methods to be explored. Palliative care is offered to terminally ill patients but historically it has not shown a great amount of success in dealing with the elevated levels of stress that accompany the illness (McCorvy, 2016). McCorvy acknowledged that 30-40% of the effectiveness of antidepressants used with this population of patients can be attributed to the placebo effect (McCorvy, 2016). Psilocybin has gained popularity as a novel and unique option for working with terminally ill patients because it has been shown to have significant antidepressant and anxiolytic effects and minimal side effects in comparison to other methods of treatment (McCorvy, 2016). Other widely used methods like SSRIs and other antidepressant medications require at least three to six weeks to achieve a clinical level of efficacy which is not ideal for patients that do not have the time to wait for results (McCorvy, 2016)

There is a growing body of evidence showing that “existential and spiritual well-being in cancer patients is associated with better medical outcomes, improved quality of life, and serves as a buffer against depression, hopelessness, and desire for hastened death” (Malone et al., 2018, p. 1). Research utilizing psychedelics for cancer patients is not new. Trials with results from hundreds of participants in the early 1960s and 70s showed improvement in depression, anxiety, fear of dying, quality of life, and pain (Malone et al., 2018). According to Agin-Liebes et al. (2020), as high as 40 percent of hospitalized cancer patients are negatively impacted by various psychiatric stressors that can develop into anxiety and depressive disorders. The conditions of the overlooked disorders are known to negatively impact quality of life, survival rates, and motivation to follow treatment strategies while increasing the rate of suicide and the will to die (Agin-Liebes et al., 2020). When an effort is made to treat these disorders the first line of

treatment involves psychotropic drugs, despite their inconsistent and limited efficacy (Agin-Liebes et al., 2020). According to Agin-Liebes et al., the lack of efficacious options for treating anxiety and depressive disorders is one of the main reasons why interest in psychedelic adjuncts to psychotherapy is once again on the rise.

In an often-referenced study, Ross et al. (2016) looked at the symptom reduction that occurs after a psilocybin session. The researchers were particularly interested in the rapidity of the reduction and how long the reduction was sustained. Unlike many studies involving psilocybin, Ross et al. were able to conduct their study using a double-blind, placebo-controlled, cross-over trial to collect their data. Their subject pool included 29 individuals with cancer-related anxiety and depression. Their subjects were randomly assigned to the group that received psilocybin or the group that received that same dosage of niacin, and both were used in conjunction with psychotherapy treatment.

The primary outcome of the study included an assessment of symptoms associated with anxiety and depression between both groups during the crossover at the seven-week mark (Ross et al., 2016). At this point in the study, psilocybin was observed to have produced immediate, substantial, and sustained improvement in feelings of anxiety and depression, which together lessened the other cancer-related feelings of demoralization and hopelessness. The results of the study also showed increases in areas that were helpful for the participants like an improved sense of spiritual well-being and overall quality of life (Ross et al., 2016).

At the six-and-a-half-month follow-up, approximately 60 to 80% of the participants showed clinically significant reductions in anxiety, depression, and other sustained benefits such as lowered existential distress, enhanced quality of life, and an improved attitude towards death (Ross et al., 2016). The researchers found that psilocybin-induced mystical experiences mediated

the amplitude of the results observed in this study. The more intense the mystical experience was for the participants the more likely they were to see significant therapeutic effects of psilocybin on anxiety and depression. These results indicate that the positive effects of psilocybin may go beyond simply reducing symptoms and impact the lives of the participants in a meaningful and significant way.

In a long-term follow-up to the Ross et al. (2016) study, Agin-Liebes et al. (2020) investigated psilocybin-assisted psychotherapy and its effects on existential and psychiatric distress in terminal cancer patients. Data was collected from 14 of the original participants 3.2 and 4.5 years following the psilocybin dosage. The study looked at anxiety and depression measures, existential stress, quality of life, spirituality, and mystical experience (Agin-Liebes et al., 2020).

The data suggested that psilocybin-assisted psychotherapy was associated with reductions in anxiety, stress, demoralization, hopelessness, and death anxiety in ways that were considered large and significant. Agin-Liebes et al. (2020) also found a continued boost in spiritual well-being at both of the follow-up dates. They found that 60-80% of the participants continued to meet the criteria for clinically significant antidepressant and anxiolytic response and remission at the second long-term follow-up. Also, 71-100% of the participants attributed the positive changes to the psilocybin-assisted psychotherapy they received. The participants reported a general sense of improved well-being and life satisfaction in connection to the psilocybin experience and rated the dosing session as one of the most personally meaningful and spiritual experiences of their lives (Agin-Liebes et al., 2020).

Although the results were strong, some limitations need to be considered. One such limitation was the cross-over design of the parent study which made it not possible to attribute

the long-term improvements directly to the psilocybin-assisted psychotherapy (Agin-Liebes et al., 2020). They cannot rule out spontaneous diminishment of distress and resolution of the disorders, or the effectiveness of other interventions, although only eight percent of the participants reported receiving any psychotherapy or pharmacological treatment since the end of the parent study.

Agin-Liebes et al. (2020) saw their results as being in support of using psilocybin to treat the often-missed existential distress among cancer patients. They also suggest that the results show promise for using psilocybin with suicidal patients dealing with feelings of extreme depression and hopelessness. Agin-Liebes et al. also saw promise in the results showing that the benefits of treating depression and hopelessness with psilocybin continued to grow over time. The greater the amount of time between the psilocybin experience and the follow-up, the more impressive the results. The researchers viewed this as particularly interesting since most treatments currently being used to treat depression and anxiety fade with time, but psilocybin results improved. The unique qualities of the psilocybin treatment set it apart from the typical medications that are being used and considering the limited efficacy of the current front-line treatments this is an exciting direction for psychiatric interventions moving forward.

In a study done by Malone et al. (2018), 13 participants previously treated in Ross et al.'s 2016 trial were interviewed to gain an understanding of possible themes related to psilocybin treatment. The researchers took an in-depth look at four participants whose experience included several of the themes reported in the key finding of the study. One participant who struggled with severe anxiety and panic attacks reported seeing geometric shapes and a spiritual guide that came into his experience through the music. During his journey, he encountered several emotional experiences and when they became too intense his guide would 'blast him' into a new

setting (Malone et al., 2018). He also encountered a divine entity that beckoned him up a mountain in what he described as a spiritual calling. Following his experience, his data showed a decrease in anxiety and an increase in spirituality and death transcendence. These findings point towards his increased feeling of acceptance which was liberating and allowed him not to worry about things that he could not change (Malone et al., 2018).

Another participant that Malone et al. (2018) interviewed spoke specifically about the music used in the session and the visual-auditory synesthesia that happened for him where he felt like he was seeing the music. His interaction with the music brought a sense of all-knowingness and a feeling of fearlessness accompanied by a transcendence from his body (Malone et al., 2018). He also explained having a feeling of overwhelming love. His data showed a moderate decrease in anxiety, depression, hopelessness, demoralization, and death anxiety. Despite the results, this participant explained that overall, he was disappointed with the results and expected a more life-changing experience (Malone et al., 2018).

Another participant had a similar experience of 'seeing the music' but also felt strong themes of unity, connection, and being at peace with death (Malone et al, 2018). She reported significant decreases in anxiety, depression, death anxiety, hopelessness, demoralization, and an increased purpose in life, spirituality, and death transcendence.

When reviewing the results, Malone et al. (2018) recognized that none of the participants had an experience dominated by any single theme. Despite having differing psychological reasons for treatment their distinct needs were met post-psilocybin treatment and sustained without any single theme standing out as the most implicative of positive results (Malone et al., 2018). There was also a list of lasting behavioural changes observed in participants such as healthier eating, increased exercise, and non-drug spiritual and/or meditative practices that were

not necessarily related to the main reasons for seeking treatment (Malone et al., 2018). Malone et al. noticed that the psilocybin experience led to deeper insight into the problems the participants were experiencing. Psilocybin may help bring about added clarity to issues being experienced by the participants and gives the therapists a better understanding of how to be supportive in a way that can integrate their experiences into successful treatment (Malone et al., 2018).

In an article by Spiegel (2016), the use of psilocybin-assisted therapy for dying cancer patients was the main focus. It has been found that enhancing feelings of self-control in a therapeutic setting is a way to boost feelings of unification and offset feelings of terror (Spiegel, 2016). Furthermore, the isolation that many terminal cancer patients face can make them feel like they are, in a sense, already dead. Being around other patients with a similar diagnosis creates a bond of life-affirming intimacy that is not possible with most other people (Spiegel, 2016). Supportive-expressive group therapy (SEGT) has been one way of working with terminally ill cancer patients to help reduce their levels of anxiety and depression (Spiegel, 2016).

Another type of therapy that was developed for the psychosocial stress and emotional distress faced by terminally ill patients was dignity therapy which has been shown to significantly improve the quality of life for cancer patients (Spiegel, 2016). Temel et al. (2010, as cited in Spiegel et al., 2016) found that early palliative care interventions that involved discussing death among patients diagnosed with lung cancer helped reduce feelings of depression and pain and extended the survival rate an extra two and a half months. Breitbart et al. (2015, as cited in Spiegel, 2016) saw how meaning-centred group therapy was able to improve the quality of life, depression, and hopelessness in patients with advanced-stage cancer. Psychotherapy for patients with advanced cancer helps to reduce feelings of depression based on the CBT

perspective that avoidance leads to phobic anxiety and the more exposure patients have the more desensitized they become (Spiegel, 2016).

Along the same lines, Nemeroff (2003, as cited in Spiegel, 2016) found that while working with individuals with major depression a combination of CBT and antidepressants showed the best results. They also found that participants of the study that were victims of childhood abuse responded to psychotherapy more than those who were not exposed to trauma and benefited more from antidepressants.

In the Spiegel (2016) psilocybin study they found that the psychedelic substance seemed to ‘reboot’ the brain in a way that sparked changes that lingered long after the drug had left the participants’ bodies. Spiegel also found similar themes between psilocybin studies and studies looking at SEGT groups. Both focus on engaging the feelings of anxiety to provoke beneficial experiences, both enhance a sense of confidence in facing challenges, and both deeply strengthen personal relationships (Spiegel, 2016). Both also involved intensified connections with life to enable an acceptance of despair related to impending death (Spiegel, 2016).

Spiegel (2016) suggests that altered states brought on through psilocybin experiences, hypnosis, and mindfulness provide enriched experiences that contrast with normal day-to-day experiences. Spiegel sees the confrontation of death as one way to enrich and savor what life you have left to live. Psilocybin increases that power of experience in a way that may help individuals gain a new perspective of self and life and free them to “go out with a bang and not a whisper” (Spiegel, 2016, p. 1217).

In another study involving terminally ill participants, Belser (2017) focused on the patient experience while being treated with psilocybin-assisted therapy. Research in this area has shown that psilocybin is associated with decreased levels of anxiety among cancer patients and

reductions in depressive symptoms for TRD patients (Belser, 2017). Psilocybin is also responsible for positive personality changes, increased openness, and profound spiritual and mystical experiences (Belser, 2017).

With these findings in mind, Belser (2017) used 13 participants from Ross et al.'s 2016 study to conduct a double-blind, cross-over, placebo-controlled pilot study to assess the efficacy and safety of utilizing psilocybin-assisted psychotherapy to treat cancer-related psychological distress. The Belser study (2017) looked specifically at measures of depression, existential/psychospiritual distress, pain, attitudes towards disease progression, quality of life, and spiritual/mystical states of mind to assess the efficacy of the therapy. The treatment was three months long and included two psilocybin sessions seven weeks apart, nine sessions of psychotherapy with two licensed therapists before and after all psilocybin sessions, and a six-month follow-up assessment.

The results from the study (Belser, 2017) suggested the importance of relational, bodily, and affective aspects in how impactful the psilocybin sessions are for the participants. Belser found that relationships were interwoven into the experiences described by the participants in the study. The participants described themes of forgiveness, reflection, and connection with loved ones that positively impacted their relationships post-treatment. Belser viewed the results as evidence that psilocybin experiences are often perceived in an emotionally embedded way that parallels different theories of human development such as attachment theory, relational theory, and interpersonal theory (Belser, 2017).

Nearly all the participants in Belser's (2017) study reported experiencing exalted feelings of joy and love in connection with their human relationships. The results also suggested that the embodiment of the psilocybin experience through alterations and transfigurations of baseline

embodied states was a unique feature of the described experiences (Belser, 2017). Some participants even experienced feelings of leaving their bodies, ejecting cancer from their bodies, or even visions of accepting their bodies as they are. Others described feelings of enhanced interoception, somatic awareness, and alterations to the felt sense of self (Belser, 2017).

This study (Belser, 2017) was able to capture the rich and complex range of emotions that are individually felt in response to the ingestion of psilocybin. Participants experienced catharsis in a powerful and healing way implying that psilocybin is a catalyst for emotionally significant experiences. The follow-up interviews described participants emerging from their psilocybin sessions with increased emotional depth and expanded affective boundaries (Belser, 2017).

The visual impact of psilocybin on the participants was another area of interest. Participants reported having colourful and complex closed-eyed visualizations that encased multi-layers of meaning for the individual and had lasting impacts on their quality of life, priorities, and overall sense of identity (Belser, 2017). During the session, participants remembered parts of themselves that had previously been forgotten. This provided them with a renewed sense of what is important, and in some cases helped them to feel more confident, connected, expansive, alive, and even reborn (Belser, 2017). It also permitted them to feel more empowered, less stuck, and more open to healthier behaviours in their post-psilocybin lives.

With all the findings in mind, Belser's study (2017) supports the conclusion that psilocybin-assisted therapy has promise for future use in areas that include individuals struggling with feelings of existential and psychological distress, such as cancer patients.

With the knowledge that anxiety and depression are often unrecognized and under-treated diagnoses for cancer patients, the positive results of studies using psilocybin are welcomed additional treatment options. Psilocybin has been shown to reduce symptoms of depression and

anxiety as well as reducing the fear of dying in a substantial, immediate, and long-lasting way. Psilocybin ‘reboots’ the brain through spiritual and mystical-type experiences that are more enriched and impactful than usual day-to-day life. It engages feelings of anxiety and depression and allows the participant to experience catharsis, healing, and connection in an emotionally significant way. The psilocybin-induced journey leads to increased emotional depth and empowerment, expanded affective boundaries, and feelings of being less stuck and more open. Post-psilocybin participants feel an improved sense of well-being after going through what is often described as the most meaningful, spiritual, and impactful experience of their lives. It is for these reasons that psilocybin-assisted therapy should be strongly considered as an addition to the repertoire of treatments involved in palliative care programs.

Psilocybin for Substance Use Disorder

Substance use disorders have historically been difficult to treat. Many abstinence programs have been unable to achieve the goal of long-term avoidance of substance use. Many programs involving the motivational interviewing stages of change model consider relapse to be one of the stages (Centis et al., 2020). In controlled studies treating smoking cessation with medication, abstinence has not exceeded 31% at the one-year mark (Johnson et al., 2016).

Smoking cigarettes is considered the most recognizable cause of avoidable premature death in the world and by simply quitting the risk of serious disease is sharply reduced (Caponnetto et al., 2017). However, quitting is anything but simple. Herzog and Bragg (2007, as cited in Caponnetto et al., 2017) found that 80% of the smokers in their study had no intention of quitting, which minimizes the chance of success since personal motivation is a major determining factor in cessation rates (Caponnetto et al., 2017). It is for these reasons that

Caponnetto et al. recognize motivational interviewing (MI) as a widely used and efficacious technique to help smokers quit even when their motivation is low.

Johnson et al.'s study (2016) included 15 participants that smoked an average of 19 cigarettes/day for a mean of 31 years and had a mean of six previous quit attempts before entering the study. The study involved a 15-week combination treatment which included four weekly preparation meetings that integrated cognitive-behavioural therapy (CBT), mindfulness training, and guided imagery (Johnson et al., 2016). In week five of the program, the target quit date (TQD), participants received a dose of psilocybin and then a second dose two weeks later. There was also an optional third high dose session offered in the 13th week.

For 10 weeks after the TQD participants submitted urine and breath samples, and self-report questionnaires as follow-up information (Johnson et al., 2016). The follow-up meeting was conducted between six months and a year after the TQD to identify potential mechanisms of change following the treatment program. The study was looking at smoking biomarkers, self-reported estimates of cigarette consumption, mystical experiences, and a persisting effects questionnaire used to monitor changes in attitudes, moods, behaviour, and spirituality attributed to the psilocybin sessions both one week and one month after the sessions.

The results of the Johnson et al. (2016) study found that 60% of the participants were biologically confirmed as smoking abstinent since the TQD. These results were a significant improvement over previous studies that used smoking cessation medications with an abstinence rate of only 31% (Johnson et al., 2016). The findings of the Johnson et al. study are consistent with other research that showed mystical-type effects and positive attributions regarding psilocybin sessions as being associated with greater smoking cessation success. The participants in the study also attributed a high degree of spiritual significance to the psilocybin sessions.

The results indicate a need for more research on the role of spirituality in quitting smoking. They also suggest a greater need to understand how the lasting behavioural and psychological shifts that occur after using psychedelics are linked to the acute effects of the 5-HT_{2A}R agonist and the mystical/transcendent experiences observed by participants (Johnson et al., 2016). The results of this study also support the use of psilocybin as part of a structured treatment program while working with other substance use disorders.

Alcohol use disorder (AUD) is widespread and affects an estimated 29.1% of American adults with life-long prevalence and 13.9% that meet the DSM-5 criteria for AUD (Garcia-Romeu et al., 2019). Current treatment for AUD consists of FDA-approved pharmacotherapies such as acamprosate, naltrexone, and disulfiram, and psychosocial treatments like screening, brief interventions, or motivational enhancement therapy (MET) (Garcia-Romeu et al., 2019). Psychosocial treatments alone, or in combination with medication, have shown limited success with upwards of 70% of individuals with AUD usually relapsing into heavy drinking within a year of the treatment (Garcia-Romeu et al., 2019). The lack of treatment success is typically associated with a higher baseline level of alcohol use severity indicators, suggesting that treatment-resistant AUD is not being treated effectively (Garcia-Romeu et al., 2019).

In a study by Bogenschutz et al. (2015) a single group within-subject design was used to deliver a 12-week, 14-session manualized intervention. Inclusion in the study required participants to have engaged in at least two days of heavy drinking in the month before the study and to be concerned about their drinking, but not currently enrolled in any kind of treatment (Bogenschutz et al., 2015). The participants also needed to be abstinent from alcohol and not in withdrawal at the time of the psilocybin sessions.

The interventions used in the Bogenschutz et al. (2015) study were psychosocial in nature. They involved 12 sessions. Seven were motivational enhancement therapy (MET), three were preparation sessions, and two were debriefing sessions. The researchers gave the first dose of psilocybin after the first four sessions and the second after four more sessions.

The results replicated other findings on the same subject matter. The most significant improvement was witnessed after the first four weeks of treatment and the first dose of psilocybin. There was a strong correlation between the intensity of the psilocybin experience and the clinical outcome for the participant (Bogenschutz et al., 2015). The researchers reported that the change in participants' drinking behaviour following the study was positively impacted by the mystical experiences that occurred during the psilocybin sessions. Bogenschutz et al. found a striking connection between the strength of the response to the psilocybin and the improvement observed in the participants. This particular finding has sparked the researchers' interest in the popular characteristics observed in psilocybin experiences and whether they are predictive of therapeutic benefit for AUD. They see this as an area that is important to pursue in future research.

The results of the Bogenschutz et al. study (2015) suggest that psilocybin may produce lasting improvements in participants suffering from alcohol use disorder. When the substance is administered in a controlled environment to patients that have been carefully selected the use of psilocybin as an adjunct to psychosocial intervention produces positive results (Bogenschutz et al., 2015). Looking at neuroimages of the brain and whether or not genetics influence the response to psilocybin could be useful directions for future research (Bogenschutz et al., 2015).

The purpose of the Garcia-Romeu et al. study (2019) was to gain a more comprehensive understanding of how non-clinical usage of psychedelics is self-reported as a useful treatment for

alcohol misuse. The data for the study was collected from participants recruited through social media websites devoted to drug discussion, education, and research. The study included individuals that met the DSM-5 criteria for AUD and had reduced or ceased alcohol use by ingesting psychedelics outside of a clinical setting (Garcia-Romeu et al., 2019). The participants were asked which mechanisms of change associated with the psychedelic use led to the changes in alcohol usage, and to compare their withdrawal symptoms against prior attempts of reducing their alcohol intake (Garcia-Romeu et al., 2019).

Garcia-Romeu et al. (2019) found that in some cases naturalistic usage of psychedelics resulted in a pronounced and enduring reduction in alcohol misuse, suggesting the potential for dramatic changes to occur. The researchers also found a congruent and significant reduction in self-reported drinks per week even though only 10% of participants reported the use of psychedelics was done with explicit intent to change their drinking behaviour. Garcia-Romeu et al. observed that even if the participants' main goal for using psychedelics was a psychological or spiritual exploration that the changes that occurred during the experience could still result in a change in drinking behaviour as well as long-lasting positive changes in relationships, diet, exercise, and work-life. The researchers found this to be the case in nearly 3/4 of the participants which coincided with other reports of long-lasting, persisting positive effects (Garcia-Romeu et al., 2019). Garcia-Romeu et al. found that 2/3 of the respondents experienced less severe cravings after the psychedelic experience which is consistent with the results in Bogenschutz et al.'s 2015 study (as cited in Garcia-Romeu et al., 2019).

Garcia-Romeu et al. (2019) suggest that serotonin 2A agonist psychedelics may possess some inherently anti-addictive properties that are mediated by the overall intensity or the mystical-type effects of the substance (Garcia-Romeu et al., 2019). Evidence from the Garcia-

Romeu et al. study suggests that the mystical-type effect combined with psychological insight might be responsible for a marked change in behaviour, such as the changes in alcohol consumption reported by the participants. The researchers also found a link between AUD, depression, and anxiety which could explain why psilocybin has shown success while working with treatment-resistant disorders.

The findings from the Garcia-Romeu et al. study (2019) are taken from participants that were self-selected volunteers that relied upon their retrospective understanding of their experience which could be subject to recall bias. Despite this obvious limitation, the results were similar to other studies and therefore still speak to the idea that psychedelic treatments are innovative, timely, and show promise for future research in this area.

The studies that have used psilocybin as a treatment for substance use disorder have been done with a small number of participants but there appears to be high consistency in the results. Bogenschutz (2016) sees consistency in the “robust and persistent long-term change in outcome measures following discrete exposure(s) to the drug, in the context of psychosocial treatment platform that both addresses the problematic behaviors/symptoms and provides a safe container for the experience” (p.4). Bogenschutz also acknowledged that safety and the lack of harmful effects observed in the studies reflect a reliable means of screening out participants that would not respond well to the use of psilocybin. Bogenschutz also found that there were certain aspects of the psilocybin experience that were predictive of the outcomes such as the intensity of the experience and the presence of a mystical-type experience.

When working with substance use disorders, psilocybin has shown results that suggest it is an effective treatment. It has been speculated that psilocybin and other serotonin 2A agonist substances could have inherent anti-addictive properties that are mediated by the intensity of

mystical-type experiences that follow ingestion. Significant mystical-type experiences provide greater insight into the problems associated with substance use and result in more observable changes in behaviour. Substance use and cravings are reduced following the use of psilocybin even when it was not the main purpose of using the substance. The use of psilocybin may be responsible for a list of positive changes such as closer relationships, improved diet, increased exercise, and a more satisfying work-life. The success seen in the psilocybin studies addressing substance use show promise for the ability to treat disorders that have been difficult to treat up to this point.

Limitations in Psilocybin Research

The main issue that hinders research using psilocybin is the absence of a placebo control group and/or an active control group (Barnby & Mehta, 2018). Since the effects of psilocybin are so pronounced it would be easy to distinguish between a placebo and a therapeutic dose of the substance.

This being the case, there is a portion of the population that is still susceptible to placebo effects as Palhano-Fontes et al. (2017, as cited in Barnby & Mehta, 2018) found when 5/15 participants in their study misclassified the placebo as ayahuasca. In another study, some participants with SUD showed an insensitivity to the psilocybin used in the experiment (Bogenshutz et al., 2015). Barnby and Mehta also recognize that without having a placebo or an active control group it is difficult to establish a proper baseline of neural activity to compare results against, which is a key area of interest in many studies. Since research suggests that certain psychedelic experiences are considered to be important parts of how psilocybin works there is a need for placebo controls that mimic some parts of the psilocybin experience but not the ones that are important to the research (Meikle et al., 2019). One way to limit the possibility

of the placebo effect when administering psilocybin to research subjects is to use two separate control compounds to minimize the chance of placebo effects (McCorvy, 2016). By including a compound that mimics some of the known effects of psilocybin, but not the ones specific to what is being tested in the study, it could provide a better understanding of which effects are related to the set and setting and which ones are psilocybin specific.

Another limitation is due to the need for support within the therapeutic setting to assure the safety of participants. This makes it difficult to tease out how much of the change is psilocybin responsible for and how much is related to the relationship with the support therapists (Barnby & Mehta, 2018). However, when working with treatment-resistant participants this is less likely the case since the failed attempts at treatment would have involved a similar level of professional support. Receiving approval to administer a schedule one substance in a study without the safety of continuous support would be unlikely making it hard to identify the key factors for change. Furthermore, Barnby and Mehta suggest that when working with depressed participants, especially in long-term follow-up studies, a natural improvement over time cannot be ruled out without having a control group included in the research.

Other issues that plague psilocybin research are the inconsistency of design, methodology, analysis methods, timing of follow-up interviews, and the overall methodological quality of the studies (Breeksema et al., 2020). Breeksema et al. concluded that the selection of participants and the expectation bias for those ingesting psychedelics might also be considered as possibly skewing the results. Although there is no lack of research findings supporting the use of psychedelic substances, there is still a lack of understanding about how psychedelic compounds contribute to the mediators and mechanisms of change in response to treatment. More work on

understanding the possible mechanisms of action is needed since knowledge in this area is still in the preliminary phase (Meikle et al., 2019).

There is also the need for research to focus on the dosing size and strategies since a simple 'one size fits all' dose would not likely be the answer when using psilocybin.

Understanding the different patterns of response over time is vital in determining what can be considered a safe dosage for therapeutic use (Meikle et al., 2019).

Meikle et al. (2019) also suggest that future studies would be wise to include more specific details about what is meant by psychotherapy. They recognize that not all therapies are created equally and believe that therapies like Acceptance and Commitment Therapy (ACT) that focus on schema change, emotional breakthroughs, and acceptance could be more appropriate for individuals that have had a psilocybin experience.

Barnby and Mehta (2018) see rigorous control conditions as necessary for any real legitimacy to be given to psilocybin research. They also see the need for control conditions to pinpoint what specific neurobiological changes are happening in psilocybin treatments. By identifying the limitations and contrasting the neural evidence between the control group studies it may be possible to highlight individual and group differences to optimize the use of psilocybin (Barnby & Mehta, 2018). According to Barnby and Mehta, the future of psilocybin studies needs to include placebo, active controls, and mechanistic evidence to encourage continued interest and support from professional bodies that fund research in this area.

Conducting research using psilocybin has had its difficulties throughout the ages. Early studies were still learning about the importance of set and setting and more recent studies despite the elevated safety measures are still hampered by the legality of the substance and the lack of interest and funding related to its legal status. The pronounced effects that take place after

ingesting psilocybin make it hard to disguise with placebo controls and limit the flexibility in how to design studies.

Despite the limitations and obstacles to generalizability, research on psilocybin-assisted therapy has shown impressive results especially in the area of treatment-resistant disorders. Anecdotal and empirical evidence both point toward psilocybin being a novel and effective treatment for a wide range of disorders that do not respond well to current treatments. The second wave of psilocybin research is still in its infancy and there is a lot to learn and discover before it is fully accepted as a legitimate and efficacious treatment, but excitement is starting to grow and the future for psilocybin looks bright.

Chapter 3

Synthesis of the Research

Psilocybin-assisted therapy is a novel approach for working with treatment-resistant disorders that have failed to respond to front-line treatments. Psychedelic substances that were once thought to be dangerous and addictive drugs are now showing promising results for TR populations. Despite the positive results in clinical trials, the stigmatized view that has kept psychedelic treatment options on the fringe continues to obstruct psilocybin from being a fully accepted and legal method of treatment.

Shifting View of Psilocybin

As interest in the potential of psychedelics continues to grow, more research can be conducted and a richer, more accurate understanding of the substance can be established. Research does not support the fear of psychedelic substances being dangerous and/or addictive. Such claims are unfounded and should no longer act as a deterrent for utilizing the potential of psilocybin in a clinical setting.

Continuing to view psychedelics as harmful and not therapeutically relevant could serve a greater purpose for those who benefit financially from the use of pharmaceutical solutions for mental health concerns. Medications that need to be manufactured and taken daily for an unknown amount of time are a more lucrative investment than a naturally occurring substance that has long-lasting effects after only one or two doses. However, with the recent legalization of medicinal cannabis and more recently recreational cannabis, a shift towards the use of natural substances with medicinal qualities could be the way of the future.

Effects of Psilocybin

The psychedelic effects of psilocybin include the magnification and alteration of a user's consciousness. Recently, researchers have discovered that these effects can help individuals experiencing TR depression, anxiety, and substance use disorders. Studies have found that post-psilocybin participants show an increase in optimism, openness, life satisfaction, and overall well-being. This increased openness may involve the dissolution of the ego and an increased feeling of connectedness within themselves, as well as with the world and the people around them. These particular changes impact the root of TR disorders in a way that other established treatments do not.

The observed effects of psilocybin are multifaceted. The therapeutic effect is achieved by the impact the substance has on the participants psychologically, cognitively, emotionally, and biologically. Psilocybin works by stimulating the serotonin receptors causing hallucinogenic effects that modulate the activity in the prefrontal network. These hallucinogenic effects fuel mystical experiences that can lead to a long-term reduction in depressive and anxiety symptoms, often from a single dose. The therapeutic change happens when the participants can achieve an increased level of acceptance in their lives after moving through challenging emotions while under the influence of psilocybin.

Therapeutic Alliance

The role of the therapist is an important one in psilocybin-assisted therapy. The ideal therapist has had their own experiences with psilocybin and has an understanding of how it works and what to expect while under the influence. Being able to learn from other experienced therapists in a mentor/mentee relationship is also beneficial. To create a welcoming environment the therapist should be able to act as a guide in a way that is participant-focused, encouraging, and aware. Similar to talk therapy, a strong therapeutic alliance can provide an added layer of

comfort and safety so that participants can experience a ‘safe trip’ with positive results. The support from the therapist encourages participants to work through and overcome any issues they may face during their psilocybin experience.

Proper pre-psilocybin preparation includes developing a therapeutic alliance, informing expectations, expanding the participants’ mental threshold for change, learning background information about the participants, strategizing how to handle potentially challenging situations, and creating a feeling of openness to the experience. For best results, the therapist should be present before, during, and after the session. During the psilocybin experience, the therapist should be available to ‘talk down’ the participants if they encounter any agitated feelings. Best results are seen in participants that are properly screened, prepared, guided, and reassured.

Environmental Considerations

How and when psilocybin is taken impacts the experience. Set and setting are contributing factors to the success of psilocybin in treating TR disorders. Although research shows that physiological risks, such as addiction, are low with psilocybin there is still the chance of psychological risk which is why participants with a history of psychosis in their families are screened out. The research shows that psilocybin can trigger an early onset of schizophrenia, with the understanding that it would have happened at some point, but the psilocybin session sped up the process. Large doses of psilocybin are not problematic as long as the participants are properly screened and prepared.

Non-pharmacological factors are important elements involved in the psilocybin experience. Best results occur when the physical setting is safe, inviting, aesthetically pleasing, and in a controlled environment. Dimmed lights, eyeshades, and carefully chosen music are all factors that improve the quality of the psilocybin session. Music played during the psilocybin

session evokes emotions and imagery while simultaneously sparking strong feelings and increasing the personal meaningfulness of the session. When the music is specifically designed to mimic the psilocybin journey it is more likely to provoke insightfulness and mystical experiences. Music tends to guide, ground, and carry the participants to psychologically different places throughout their experience. The most effective genres of music seem to be ambient, classical, and traditional/ethnic. In research, participants that were the most receptive to the music found that it activated more emotions, thoughts, and memories that were personally salient.

Post-Psilocybin Session

Post-psilocybin the importance shifts to the follow-up. Much of the post-psilocybin work is geared towards reflection and working through the experience using talk therapy. The mystical-like experiences that happen while using psilocybin are predictive of positive outcomes for participants. The mystical-like experiences seem to have an integrative and antidepressant effect. The ability to surrender to the experience is helpful throughout the entire process. Follow-up sessions allow the participants to debrief, work through, and integrate what they learned and experienced during the psilocybin session. When the psilocybin experience includes feelings of absorption, spiritual motivation, openness, and surrender participants described the session as spiritual and highly memorable.

Talk therapy as an adjunct to psilocybin therapy is best utilized when the participants are feeling a strong sense of connection and acceptance post-psilocybin session. Working with participants when neuroticism levels are low allows them to experience more openness, extroversion, and conscientiousness and feel less isolated and depressed. The change in the participants is fast and is considered by some as a ‘quantum change’ (Erritzoe et al., 2018).

When participants experience the psilocybin session in a spiritual manner, they notice an increased level of extroversion that may be expressed through profound insights they observed while under the influence.

Psilocybin and TR Disorders

Psilocybin appears to work through novel mechanisms of change. The substance ‘lubricates the mind’ and increases the signal to the serotonin 2A receptors which makes new ways of thinking more accessible to the user. Researchers have taken notice of its long-lasting effects, its low potential for addiction, and its ability to treat TR disorders in a way that pharmaceuticals have failed to do. Flexible cognition results from the global network disintegration and anti-inflammatory effects that accompany the psilocybin dose. Feelings of oceanic boundlessness increase, and the dread of ego dissolution dissipates. The focus of thought shifts from being self-centred to socially-centred. As their minds ‘expand’ participants feel more free and less stuck. Participants in psilocybin studies showed more emotional empathy and were better able to consider the values and worldviews of others while thinking in less ego-driven ways.

When used with cancer patients, psilocybin increased levels of spiritual well-being while decreasing cancer-related anxiety, depression, and existential distress. Post-psilocybin, cancer patients perceived an improved quality of life, showed a more accepting attitude towards death, and exhibited healthier behaviour overall. The psilocybin experience also enhanced their feelings of control in their lives. It is thought that engaging the feelings of anxiety while under the influence of psilocybin can provoke a more beneficial experience, enhance patients’ confidence to face challenges in their lives, and strengthen existing relationships they have with loved ones.

When using psilocybin to work with TR substance use disorders the mystical-like effects seemed to be the most impactful. For example, the positive attributes associated with mystical-like experiences correlated with an improvement in the rate of smoking cessation (Johnson et al., 2016). The more intense the spiritual nature of the psilocybin experience the more impressive the results were. The positive effects were not limited to a decrease in the use of substances but also included a general improvement in the participants' lifestyle, such as an improved diet and increased exercise. Those who were able to abstain from the use of substances also experienced fewer cravings post-psilocybin. It is thought that psilocybin may have an inherent anti-addictive quality since recreational psilocybin users have reported experiencing a drop in their consumption of alcohol even when that was not the purpose for ingesting psilocybin. The overall results were impressive when psilocybin was used with TR substance use disorders, but the best results came when the mystical experiences brought on deep insights for the participants to fold into their lives.

Important Information for the Public

In the late 1960s and early 1970s psychedelic substances went from the subject of promising government research to a schedule one banned substance. Psychedelic substances were villainized and said to be highly dangerous and addictive with little to no evidence to support these claims. Now that they are once again a topic of focus for cutting-edge treatments in the field of mental health, the truth about psychedelics is starting to become known. A review of the literature on psilocybin use in a clinical setting supports their use with properly screened and prepared participants. Psilocybin is neither dangerous nor addictive, but rather the opposite. Even the administration of large doses of psilocybin did not result in any dangerous results, and when

used with individuals suffering from TR substance use disorder psilocybin showed indications of natural anti-addictive properties.

In comparison to other pharmacological options for treating TR disorders, psilocybin has fewer side effects, less addictive qualities, and has more long-term effects from a single dose. The effects of psilocybin extend beyond symptom reduction to a more general feeling of well-being. Many participants in psilocybin studies consider the experience while under the influence to be significant, highly memorable, and even life changing.

Individuals who are considered treatment-resistant have been suffering for a long time and are willing to try almost anything in search of relief including alternative treatments like psychedelic therapy. Research on psilocybin-assisted therapy has shown a large and positive impact after a single dose which is a welcomed alternative to more invasive options like ECT. The false narratives around psychedelic substances interfere with the accessibility of psilocybin-assisted therapy and act as a deterrent to individuals who are desperate for results but remain concerned about the attached stigma.

As more information is collected about the potential uses and benefits of psilocybin the public should get a more accurate and understanding view about psilocybin-assisted therapy. As the public becomes better informed on the subject the barriers that keep psilocybin-assisted therapy on the fringe will begin to disappear, setting the stage for a more progressive and empathetic view of how best to work with TR disorders in the future.

Recommendations

As I have reviewed the research on the topic of psilocybin-assisted therapy I have gained a better understanding of the best practices that should be considered when organizing an

effective treatment plan for TR clients. In the following section, I will outline my recommendations for a psilocybin-assisted therapy program for clients with TR disorders.

Screening

Proper screening is important to identify which clients have a family history of schizophrenia and would be at risk for a psilocybin experience to act as a catalyst for an early onset of the disorder. The screening does not need to be as stringent as it was in some psilocybin research that screened out individuals with high levels of rigidity as long as the clients are properly prepared for the psilocybin experience.

Preparation

Including preparation sessions before the date of consumption is important. Best results are achieved when participants are in the right mindset to fully benefit from what the psilocybin journey has to offer. Entering into the psilocybin session with a negative and/or rigid mindset can result in a ‘bad trip’ or a less impactful experience if the participant is not open and/or receptive. Since psilocybin is an amplifier of existing thoughts and feelings, going into the experience with a positive mindset makes a difference. Preparation also includes familiarizing the participants with what could happen for them along the journey. Equipping the participants with a level of expectation can help with feelings of anxiety and fear that can be paired with unfamiliarity.

Empathetic, Knowledgeable, and Experienced Therapists

Research has shown the importance of the therapeutic relationship in the effectiveness of psychotherapy. This is also true for psilocybin-assisted therapy. Best results come when participants are comfortable with and trusting of the therapist. Having a therapist that is knowledgeable about the effects of psilocybin and is familiar with what happens during a psilocybin session through their own experience puts the participants in capable hands. An

empathetic, knowledgeable, and experienced therapist has a better understanding of what the client is going through and can be there for them in a supportive and understanding way.

Calm, Safe, and Inviting Environment

Setting has a strong impact on the psilocybin experience. The psilocybin experience involves high levels of emotionality which may include participants facing their fears along the journey. Having a safe place to start from and end provides the security needed to muster up the courage to face the challenges that may present themselves during the experience. For these reasons creating a calm, safe, and inviting environment is important. I would recommend a room with a choice of furniture options, such as a reclining easy chair or a comfortable couch. I would suggest soft lighting fixtures such as Himalayan salt lamps or something similar. Decorating the room minimally with art pieces that are pleasing to the eye could add to the relaxing and calming ambiance. I would also suggest scented candles or a diffuser to give the room a faint but pleasant smell. It would be best to let the participants decide on the scent beforehand to avoid any aversions they may have to particular smells. Many of the studies also used eyeshades which I agree is a good option so the client can focus on the hallucinogenic effects of the psilocybin without the added task of making sure they keep their eyes closed. Finally, I would suggest having some clean and comfortable blanket and slipper options available for participants that would appreciate the extra feelings of comfort.

Music

When the right music is used during the psilocybin session it has been shown to positively impact the experience for the user. Music that mimicked the different stages of the psilocybin experience and resonated with the participants was able to provide a new dimension to the journey and contributed to the success of the treatment. Part of the preparation before the

dose sessions should include working with the client to choose which one of the music options available is the best fit for them. Research suggested that genres such as ambient, neoclassical, or ethnic/traditional music work well to set the stage for a meaningful psilocybin experience.

Dose Size

The size of the psilocybin dose used in psilocybin-assisted therapy does not change the level of safety for the client but it does impact the intensity of the experience they may have while under the influence. The optimal dose in a therapeutic setting is big enough that it brings on the hallucinogenic effects but small enough that the intensity is not too much for a first-time user. Even properly prepared participants could experience a ‘bad trip’ if they ingest an unexpectedly strong dose of psilocybin. With 30 mg considered to be a large dose and 10 mg considered to be a small dose, the 20 mg dose seems to be the ‘sweet spot’ for psilocybin doses in a therapeutic setting.

Check-In

On the day of the psilocybin session, it is important to check in with the client to make sure they are in the right headspace to go ahead with the psilocybin portion of the treatment. Proper preparation aside, the mindset on the day is something that should be considered and monitored before deciding whether or not to proceed with the psilocybin experience.

Continuous Therapist Support

Having the therapist present and available during the psilocybin session is a way to maintain a level of safety and security for the client. Having a knowledgeable and supportive therapist to refer back to during times of increased anxiety or intensity is a helpful way to anchor the client to reality when they are at risk of being overwhelmed by the hallucinogenic effects of the psilocybin.

Debriefing

To solidify the changes that happen for the participants it helps to provide them with a safe place to debrief about what they experienced while under influence of psilocybin. A trained therapist who is familiar and experienced with psilocybin and can empathize and connect with the participants in a way that someone who has not experienced the effects of psilocybin is incapable of. Being able to speak openly and honestly about the psilocybin experience allows the client to internalize the experience in a meaningful and impactful way.

Consolidating Activities

Although it was not something that I saw specifically mentioned in any of the studies included in this paper, I believe that some type of consolidation activity could be an effective way of solidifying the memory of the psilocybin experience that goes above and beyond debriefing. Encouraging participants to write, draw, and/or paint about their experience is a way to capture and solidify the feelings that came up and shape them into long-term memories. Engaging in such activities could allow participants to express their feelings in a way that might not be accessible through talking, even if it's with a qualified therapist.

Post-Psilocybin Talk Therapy

Particularly with TR individuals, post-psilocybin talk therapy is a chance to engage with profound insights that have arisen from the psilocybin experience and to work with the new ways of thinking available after the post-psilocybin brain 'reset'. The increased feelings of openness allow for a new level of work to be achieved in a therapeutic setting. Having the chance to process and unpack what happened during the psilocybin-assisted internal journey can solidify the memories and the self-realizations that occurred while under the influence of psilocybin. Together, participants and therapists can reap the benefits that accompany what has been referred

to by many as the most profound and meaningful experience of their lives (Agin-Liebes et al., 2020). Cultivating the short-term effects into long-term effects can pay dividends for the participants in their lives moving forward.

Future Directions

The recent re-emergence of research involving psychedelic substances is a welcomed direction for future treatment options, not only for TR individuals but for any individual who recognizes the potential in psychedelic therapy. With research in this area being nearly obsolete for almost three decades, there are still many areas of interest that have not yet been broached. In this final section, I will be looking at future directions for psilocybin research.

Micro-Dosing Psilocybin

Micro-dosing was not a focus of this paper, but it is a subject that I came upon a few times in my research. Micro-dosing is the use of psilocybin in small, sub-hallucinogenic doses. The idea of micro-dosing is to capture the benefits associated with psilocybin while avoiding the four to six-hour hallucinogenic experience. It is an area that shows promise for a number of different reasons. Micro-dosing could be a more accessible option for individuals that are not interested in or might not respond well to the hallucinogenic effects of psilocybin. Large doses of psilocybin can provide one of the most important experiences of a participant's life, but it is not an experience that everyone is seeking.

Positive Psychology

Using psilocybin as a way of promoting positive psychology is an idea that has been mentioned in several studies. The positive impact of psilocybin has been observed in the reduction of TR disorder symptoms, as well as increasing feelings of general well-being in individuals that ingested psilocybin. The idea is that psilocybin can be used to pre-emptively

target mental health issues before they have the opportunity to develop. For example, psilocybin can disrupt patterns of rumination and rigid ways of thinking before they become too deeply entrenched and present themselves in a disordered way. Utilizing psilocybin as a way to encourage individuals to be more open and less closed off from themselves and others can provide a sense of connection that is missing for many who are experiencing disordered ways of thinking.

As mentioned earlier, the effects of psilocybin do not begin and end with the ability to alleviate problematic symptoms. The benefits extend to broader areas outside of the main reasons for psilocybin-assisted therapy. A general sense of well-being was observed in a number of studies involving psilocybin. Increased spirituality, healthier eating habits, more exercise, and improved relationships with friends and family were all observed alongside the main focus of the studies. These are areas that individuals at all points along the spectrum of mental health could find useful in their lives.

With this in mind, using psilocybin with healthy populations could make sense from a preventative perspective on mental health. Psilocybin is a non-addictive substance that can have a lasting impact from a single dose. It is a substance that can be used as an adjunct to other self-improvement strategies to promote an overall state of mental and physical wellbeing.

Types of Therapy

The research that I reviewed on psilocybin-assisted therapy did not go into great detail about which approach to therapy is best following a psilocybin experience. There was mention of the added benefit of combining mindfulness meditation with psilocybin therapy, suggesting that ACT therapy could prove beneficial, but this has not yet been tested in a clinical setting.

The lack of research in this area could mean that the type of therapy is not so important as long as it helps integrate the experience into the lives of the psilocybin participants. The resurfacing of psilocybin research in the field of mental health is a recent development, so it stands to reason that preliminary research is more interested in understanding how and why psilocybin works with the different disorders before they focus on which style of therapy is best suited for psilocybin-assisted work. This is an area that I think is important moving forward as a way to fine-tune the best approaches to target the issues that each individual is dealing with.

Mechanisms of Change

The understanding of which mechanisms of change are involved when using psilocybin is still in its infancy. It is known that psilocybin and other psychedelics target the serotonin 2A receptors with their hallucinogenic qualities, and it is known that psychedelics alter ways of thinking in a more positive direction. However, much is still unknown about why psilocybin is successful in treating depressive, cancer-related, and substance use disorders in the way that it does. It raises the question of what other hard-to-treat disorders could be treated with psilocybin?

Furthermore, since psilocybin research has only recently come back into favour, many research results have not yet been replicated. There is still a lot to be learned about how psilocybin and other psychedelic treatments could be used to help individuals who are not getting the results they seek with the current treatments available to them.

Gaining Wider Acceptance

Research in the 1950s and 60s was already showing promising results from the use of psychedelic substances before they were made illegal and put on the schedule one banned substance list. After decades away from the mainstream, interest in the therapeutic use of psychedelics re-emerged in the late 90s. Its reputation as an illegal drug made it difficult to get

approval to conduct research and examples of its treatment success were still largely downplayed and ignored by many working in the field of mental health. Even now, with positive momentum building behind it as a breakthrough in mental health treatment, the public perception of psychedelic substances is shifting, but for those working in mental health, for the most part, the opinion continues to be one of skepticism and disapproval.

Several obstacles continue to stand in the way of psilocybin being fully accepted as a novel and effective treatment for mental health disorders. As previously mentioned in this paper, researchers and research funders are hesitant to give psychedelics their full support for fear of ruining their reputation by working with stigmatized substances. Pharmaceutical companies also fail to see how a naturally occurring substance like psilocybin that has shown long-term effects after a single, small dose can be a profitable endeavor for them to invest in.

Until the shift in the public's opinion of psychedelics is mirrored by lawmakers, research funders, pharmaceutical companies, and mental health professionals, psychedelics and more specifically psilocybin will continue to be on the outside looking in. Novel mechanisms of change make these substances unique and effective in their ability to treat TR disorders in ways that current treatments are unable to. Finding new and effective ways to address mental health concerns should be prioritized above all else. If the goal is to find ways to improve the lives of individuals experiencing mental health disorders, then psilocybin-assisted therapy should have a bright future ahead.

Final Thoughts

Globally, mental health concerns continue to be on the rise. It is not something that is going away any time soon. With this reality in mind, mental health professionals who truly care about the well-being of the individuals they work with should be in support of research seeking

the best ways to provide treatment to those in need. Despite its history, psilocybin research is showing promising results, especially while working with TR disorders. To continue to live in the past and perpetuate the belief that psilocybin is dangerous, addictive, and should remain a banned substance is a disservice to the potential of the substance and to the individuals that are currently being under-treated.

My hope for the future of psilocybin and psilocybin-assisted therapy is one of acceptance and innovation. The research in this area highlights a substance that can have lasting effects in hard-to-treat areas after a single dose. To dismiss and deny the need and potential effectiveness of such a treatment based on past misinformation would not reflect well on the field of mental health, which is centred around helping people. I am encouraged by the changing perspective of the general population and I am optimistic that mental health services will follow suit. Individuals should be aware of the different treatment options that are most efficacious in their area of need and should be permitted to make their choices free of stigma from uninformed sources. This is the future for psilocybin that I look forward to.

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